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BRONCHIAL OBSTRUCTION AND TRACHEOBRONCHIAL TUBERCULOSIS*

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BOSTON

SINCE the careful studies of Clerf,[1] Eloesser,[2] and Samson,[3, 4] bronchoscopy in tuberculosis has been found to be increasingly important. In the early days it was thought that this procedure would be hazardous to the tuberculous patient and might result in spreading the infection, but this has not proved to be the case. On the contrary, knowledge concerning the presence or absence of disease in the tracheobronchial tree obtained by the use of the bronchoscope has been of great aid to the internist and thoracic surgeon in planning treatment.

Tracheobronchial tuberculosis may take three principal forms: the ulcerative, in which there is a diffuse or circumscribed loss of mucosa; the hyperplastic, where there is submucosal proliferation and sometimes the formation of conglomerate tubercles; and the stenotic, in which there is definite scar-tissue formation leading to partial or complete bronchial obstruction.

The indications for bronchoscopy in tuberculosis are as follows: obstructive signs and symptoms as shown by atelectasis, wheeze, difficulty in raising sputum, persistent cough or dyspnea and intermittent febrile attacks; positive sputum when parenchymal disease is controlled or absent; hemorrhage, unexplained by parenchymal disease; and contemplated collapse therapy to determine the possible presence of tuberculosis in the trachea or contralateral bronchus.

In a previous paper[5] I called attention to 4 cases having symptoms of intermittent bronchial obstruction following thoracoplasty, all of which were relieved by bronchoscopic aspiration of secretions with bougienage. One patient in this group later required lobectomy.

Tuberculous stricture of the bronchus following thoracoplasty may produce an almost complete obstruction, which can often be markedly relieved by repeated bronchoscopic dilatation.

Since there are many other causes of bronchial obstruction, let us first consider the differential diagnosis. The clinical history, together with the x-ray and laboratory findings, may often lead to a correct presumptive opinion concerning the cause of bronchial obstruction, but in the last analysis only direct bronchoscopic study with biopsy of the lesion will give the final histologic diagnosis. As examples the following cases are cited.

CASE 1. G. E. H. (M. G. H. U216741), a 27-year-old man, first entered the hospital because of cough and hemoptysis of 10 months' duration. X-ray examination (Fig. 1) showed complete atelectasis of the right lung.

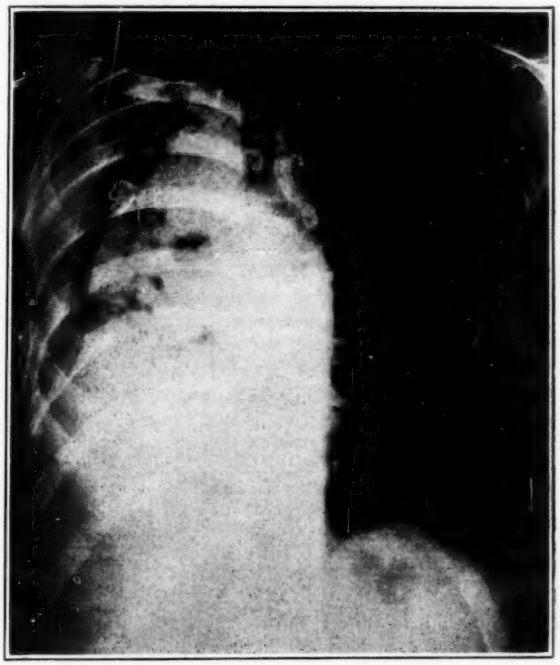

FIGURE 1. *Case 1.*

Atelectasis of right lung; presumptive diagnosis, adenoma; bronchoscopic biopsy, epidermoid carcinoma, Grade III.

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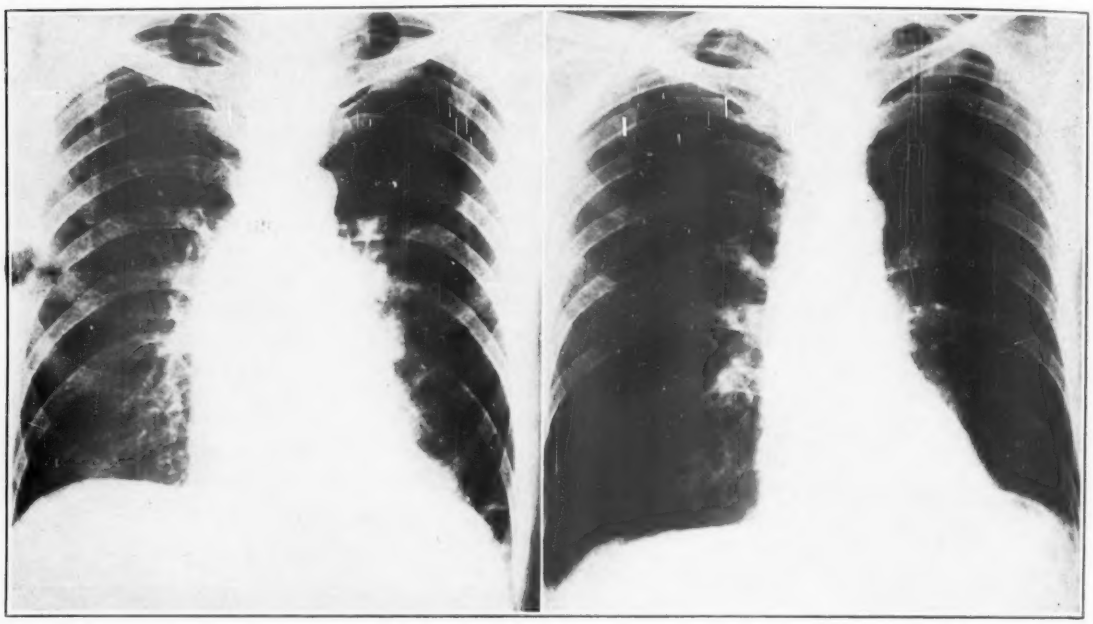
Because of the patient's youth the presumptive diagnosis was benign adenoma of the right main bronchus. Bronchoscopy,* however, revealed a malignant tumor, which was biopsied and reported as epidermoid carcinoma, Grade III.

Case 2. W. M. R. (M. G. H. U224885), a 56-year-old man, entered the hospital complaining of cough and hemoptysis of 1½ years' duration. X-ray examination (Fig. 2A) showed a mass in the left hilus with collapse of the left lower lobe. Because of the patient's age the presumptive diagnosis was bronchogenic carcinoma. Bronchoscopy, however, showed a smooth, round, lobulated tumor arising in the left-lower-lobe bronchus. A biopsy specimen was reported as benign adenoma. Following bronchoscopic removal the patient has remained essentially symptom free for the past 2½ years. The collapse of the left lower lobe persists but the mass in the left hilus has disappeared (Fig. 2B). The bronchoscopic appearance of the adenoma is shown in Figure 3.



A B

Figure 2. *Case 2.*

A — *Collapse of left lower lobe, with a mass at left hilus; presumptive diagnosis, carcinoma; bronchoscopic biopsy, benign adenoma.* B — *Following removal of adenoma, persisting collapse of left lower lobe, without hilar shadow; patient asymptomatic.*

A rare cause of bronchial obstruction is metastatic tumor.

Case 3. W. C. P. (M. G. H. U30702), a 42-year-old man, first entered the hospital in 1938, at which time a sarcoma of the testicle was removed. Nine months later he was readmitted because of bronchial obstruction with collapse of the left lung. X-ray examination (Fig. 4) showed masses in the right-lung field consistent with metastatic tumor and a complete collapse of the left lung. Bronchoscopy demonstrated a ragged tumor mass obstructing the left main bronchus, a biopsy of which led to a report of metastatic sarcoma. Following partial bronchoscopic removal there was temporary improvement, with some re-expansion of the left upper lobe.

Another cause of partial bronchial obstruction is sarcoid. In a case previously reported,[6] the chief complaints were dyspnea and wheeze. The chest x-ray finding was that of sarcoid. Bronchoscopy showed sarcoid involving the carina and both main bronchi, confirmed by biopsy. There was definite improvement following bronchoscopic removal of the tissue and secretions.

The following cases illustrate different manifestations of tracheobronchial tuberculosis.

Case 4. A. R. (M. G. H. U84531), a 29-year-old woman, gave a 7 years' history of tuberculosis, with cough and positive sputum. She had had a left phrenicectomy.[4] During the previous year there had been intermittent periods of fever, with increased cough and sputum. X-ray examination (Fig. 5) showed complete collapse of the left lung with cavitation. At bronchoscopy, almost complete obstruction of the left main bronchus 2 cm. below the carina was demonstrated. The stricture was smooth and no ulceration was seen. It was dilated by the passage of esophageal bougies (sizes 8 to 12). No follow-up was obtainable, as the patient lived at a distance.

This patient had a positive sputum, and bronchoscopy confirmed the presumptive diagnosis of tuberculous stricture.

*All bronchoscopies were performed by me except those in Cases 9 and 10, performed by Dr. Lowrey F. Davenport, and the first bronchoscopy in Case 14, performed by Dr. Ralph H. Adams.

Case 5. C. M. D. (M. G. H. U346536), a 26-year-old woman, gave a long-standing history of pulmonary tu-

Figure 3. *Case 2.*
Bronchoscopic appearance of multilobular benign adenoma.

berculosis and tuberculous laryngitis, with positive sputum. She had been treated by partial right pneumothorax and left oleothorax. X-ray examination (Fig. 6) showed the

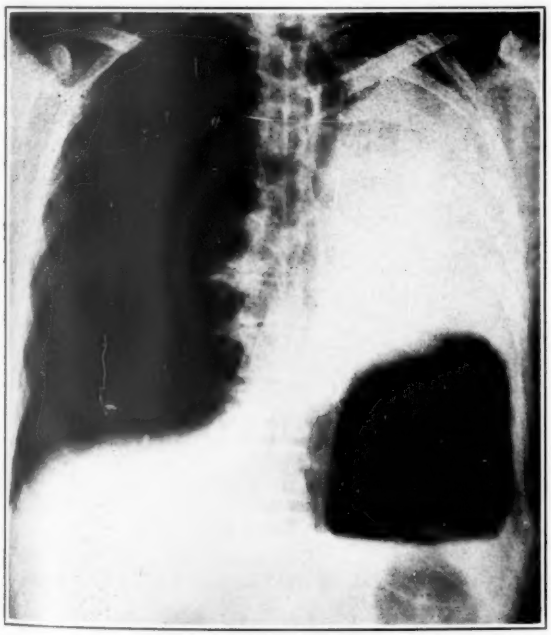


Figure 4. *Case 3.*
Atelectasis of left lung due to sarcoma of bronchus, metastatic from testicle; metastatic disease also in right-lung field.

right lung half collapsed and herniated across the midline. There was oil on the left side and possible partial occlusion of the left main bronchus. At bronchoscopy the left main bronchus 2 cm. below the carina was narrowed to a 3-mm. lumen. The stricture was smooth and fibrous. It was dilated by the passage of esophageal bougies (sizes 12 to 16). There were no retained secretions. A smear taken from the stricture showed tubercle bacilli.

Case 6. A. W. P. (M. G. H. U329952), a 38-year-old man, entered the hospital because of chronic cough and positive sputum. X-ray examination (Fig. 7) showed partial collapse of the right upper lobe, with probable cavitation and stenosis of the right-upper-lobe bronchus. Bronchoscopy domonstrated reddening and almost complete stenosis of the right-upper-lobe bronchus, with two pin-point tubercles (Fig. 8). The stenosis was best seen by the use of the right-angle telescope[7, 8] (Fig. 9). Since the disease was confined to the right upper lobe and ir-

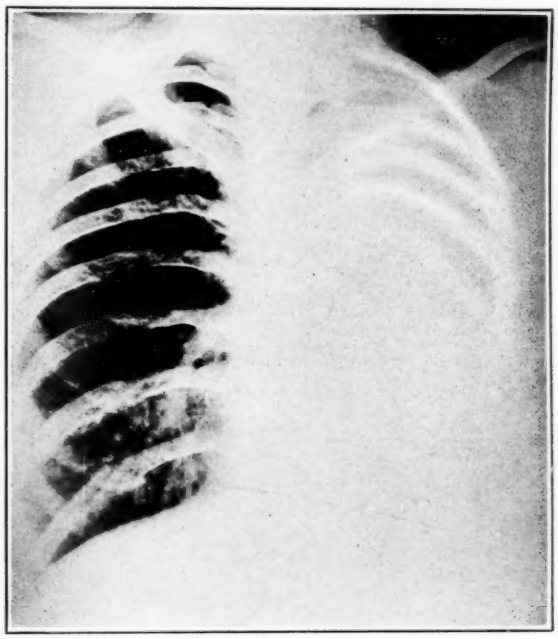


Figure 5. *Case 4.*
Atelectasis of left lung; positive sputum; tuberculous stricture of left main bronchus.

reparable damage to this lobe had already occurred, lobectomy was performed by Dr. E. D. Churchill, with success. The pathologic specimen showed no cavitation but moderate bronchiectasis, with very extensive microscopic bronchial tuberculosis throughout the lobe. The patient made a satisfactory recovery and has been essentially symptom free for 7 months since the operation.

In the above 3 cases positive sputum for tuberculosis made the diagnosis fairly obvious. In some of the following cases, however, the sputum was negative and the diagnosis was more obscure.

Case 7. V. D. (M. G. H. U253261), a 28-year-old woman, entered the hospital complaining of cough, fever and chills of 1 year's duration. The sputum had been negative for tubercle bacilli on ten examinations. X-ray examination (Fig. 10) showed calcified lymph nodes and collapse of the right lower lobe. The X-ray Department made a tentative diagnosis of tuberculosis in spite of the negative sputums. Bronchoscopy revealed distortion of

the right bronchial tree with outcropping near the bifurcation of the lower lobe. The biopsy diagnosis was tuberculosis. Pneumonectomy was later performed by Dr. Richard H. Overholt.

CASE 8. M. L. K. (M. G. H. U271988), a 59-year-old man, entered the hospital because of recurrent attacks of hemoptysis. The sputum on several occasions had been negative for tuberculosis. X-ray examination (Fig. 11) showed probable tuberculosis of the left upper lobe, with bronchiectasis. Bronchoscopy, however, revealed a 7-mm. ulcer of the *right* stem bronchus, the ulcer having sharp margins and a dirty base. A smear taken from the ulcer was positive for tuberculosis. A year and a half later

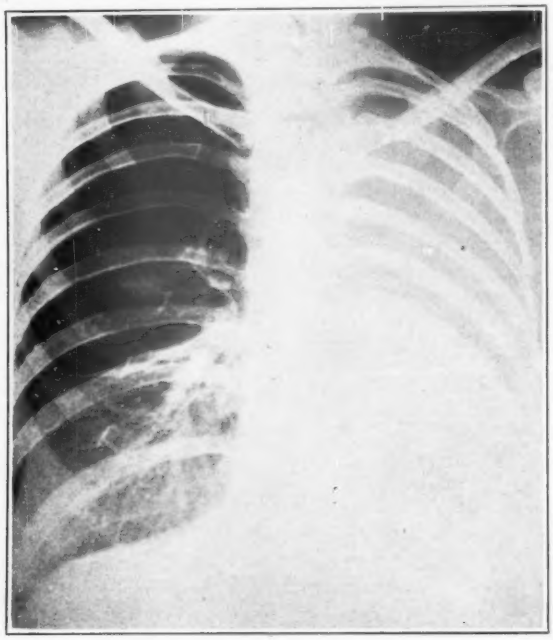


FIGURE 6. *Case 5.*

Partial collapse of right lung, with pneumothorax; herniation of right lung across the midline; left oleothorax; positive sputum; tuberculous stricture of left main bronchus.

the patient's physician reported that he was getting along satisfactorily under medical care.

It is noteworthy in this case that most of the disease was assumed to be in the left upper lobe, but bronchoscopy showed an active, ulcerating lesion in the right stem bronchus. Information of this sort is naturally of very great importance, especially if any surgical treatment is contemplated. Moreover, bronchoscopy in this case, as in Case 7, was the only method of examination to yield a positive diagnosis.

CASE 9. T. F. (M. G. H. U205925), a 28-year-old woman, entered the hospital with a 3-year history of cough, fever and wheeze. Left pneumothorax had been necessary every 6 weeks. Tubercle bacilli had never been found in the sputum on repeated examinations. X-ray examination (Fig. 12) showed complete collapse of the left lung, with cavity formation. Bronchoscopy demonstrated that the left main bronchus was completely occluded by a red, elevated, fungating mass, from which a biopsy was obtained, the pathological report being tuber-

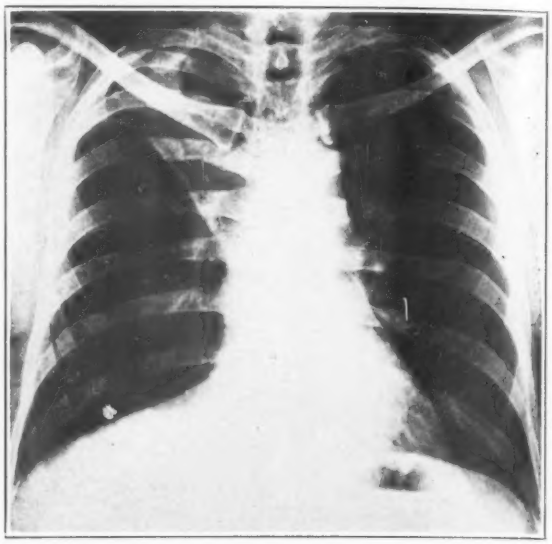


FIGURE 7. *Case 6.*

Partial collapse of right upper lobe, with cavitation; positive sputum.

culosis. Eight months later a second bronchoscopy showed the left main bronchus almost completely stenosed and represented by only a small dimple in the mucous mem-

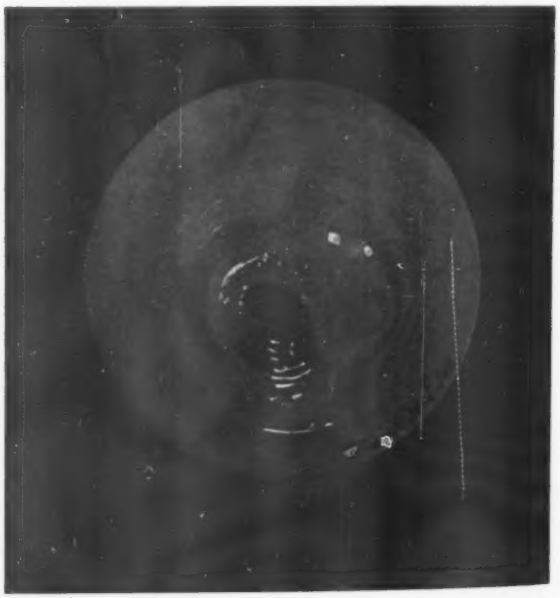


FIGURE 8. *Case 6.*

Bronchoscopic appearance of right-upper-lobe orifice as seen with right-angle telescope; almost complete stenosis of orifice, with two pin-point tubercles just proximal to the stenosis.

brane of the trachea. There was no evidence of tuberculosis in the trachea or right main bronchus. Accordingly, Dr. Churchill performed a left pneumonectomy. Unfortunately, however, in spite of all precautions taken, the

disease progressed in the right lung and the patient died 1½ years later.

Cases 7, 8 and 9 illustrate the importance of bronchoscopy in establishing a positive diagnosis of

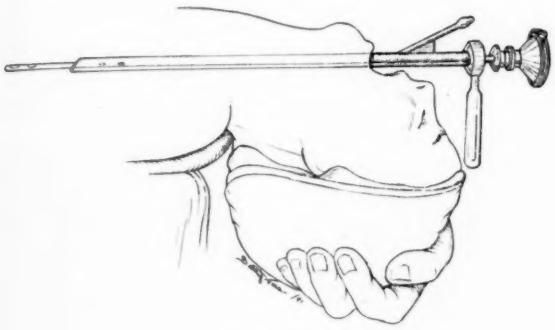


FIGURE 9.

Diagram showing technic of introducing telescope with right-angle vision through a standard bronchoscope for inspection of upper lobes.

tuberculosis when all sputum examinations have been repeatedly negative.

CASE 10. J. J. McC. (M. G. H. U46518), a 43-year-old man, entered the hospital with a 20-year history of cough

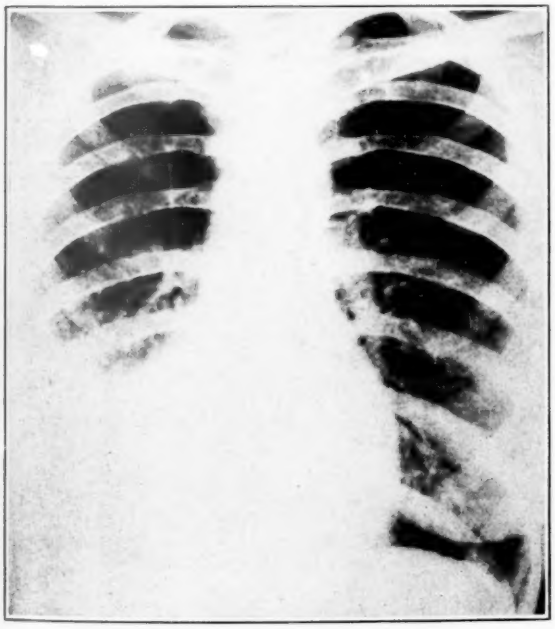


FIGURE 10. *Case 7.*

Atelectasis of right lower lobe, with calcified lymph nodes; negative sputum; bronchoscopic biopsy, tuberculosis of right-lower-lobe bronchus.

and a 6-month history of hemoptysis. Sputum was expectorated up to a cupful each day and had several times been positive for tuberculosis. X-ray examination (Fig. 13) showed a mass at the right hilus, with cavitation. Because of the positive sputum, tuberculosis was considered likely, although carcinoma was also mentioned. Bronchoscopy revealed an irregular, fungating mass near

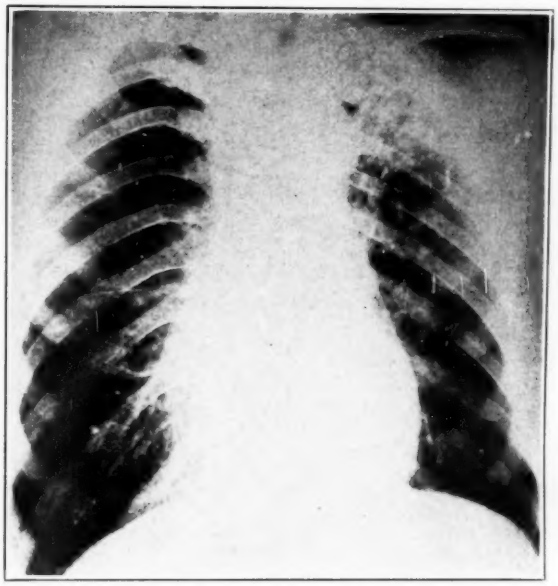


FIGURE 11. *Case 8.*

Probable tuberculosis of left upper lobe; negative sputum; bronchoscopic examination, 7-mm. ulcer of right stem bronchus; bronchoscopic smear from ulcer; positive.

the right-middle-lobe orifice; the biopsy diagnosis was epidermoid carcinoma, Grade IV. Pneumonectomy was

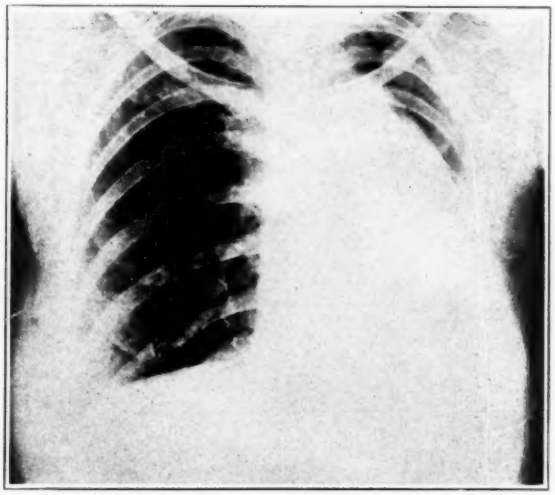


FIGURE 12. *Case 9.*

Atelectasis of left lung; sputum negative; bronchoscopic examination, fungating mass in left main bronchus; bronchoscopic biopsy, tuberculosis.

therefore performed by Dr. Churchill. Five years later the patient was fairly comfortable, although complaining of some dyspnea and cough.

In this case clinical evidence pointed chiefly to tuberculosis, but bronchoscopy disclosed a bronchogenic carcinoma in addition to the tuberculosis.

CASE 11. M. E. W. (M. G. H. U189707), a 57-year-old woman, entered the hospital complaining of wheeze of 2 months' duration. There was almost no cough or sputum. Sputum examinations on several occasions were negative for tuberculosis. X-ray examination (Fig. 14) showed complete collapse of the left upper lobe and partial collapse of the left lower lobe. The findings were interpreted as being possibly due to carcinoma, although the pointed extremity of the left main bronchus and numerous calcified glands raised the possibility of a benign tuberculous stricture. Bronchoscopy (Fig. 15) showed multiple tubercles extending down the left main bronchus all the way from the carina to the partial stenosis. A guinea pig inoculated with bronchoscopic aspiration developed tuberculosis. X-ray treatment was given, with definite improvement. Three years later the patient re-

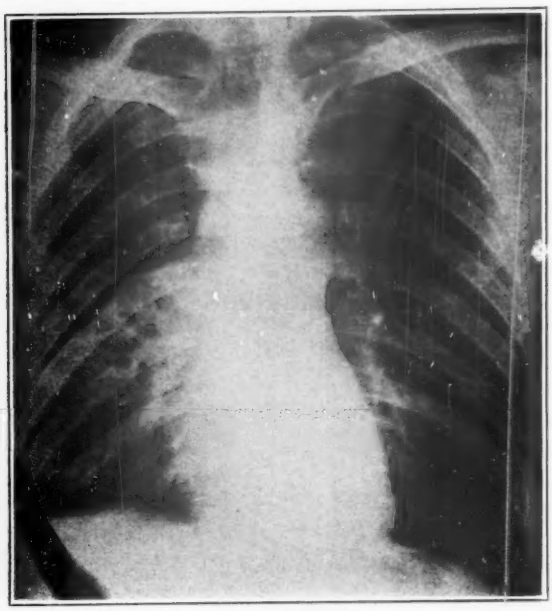


FIGURE 13. *Case 10.*

Right hilar mass, with cavitation; positive sputum; bronchoscopic biopsy, epidermoid carcinoma, Grade IV.

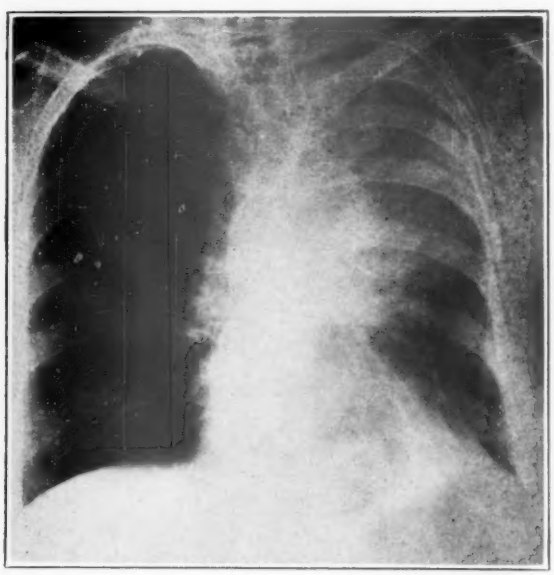


FIGURE 14. *Case 11.*

Atelectasis of left upper lobe; partial atelectasis of left lower lobe; sputum negative; bronchoscopic examination, multiple tubercles in left main bronchus; bronchoscopic aspirations, positive in guinea pig.

FIGURE 15. *Case 11.*

Bronchoscopic appearance of multiple tubercles in left main bronchus, showing left-upper-lobe orifice and subdivisions of left lower lobe.

FIGURE 16. *Case 12.*

Atelectasis of right lower and right middle lobes (portable film); clinical diagnosis, bronchogenic carcinoma with brain metastases; bronchoscopic biopsy, acute and chronic inflammation (? tuberculosis); subsequent sputum positive.

ported no further upsets, no cough, negative sputum and some wheeze. X-ray examination showed fibrosis of the left upper lobe.

In this case bronchoscopic examination resulted in a positive diagnosis of tuberculosis, for which x-ray treatment was subsequently given.

Case 12. B. F. (M. G. H. U235515), a 62-year-old woman, entered the hospital complaining of 2 years' wheezing, 4 days' fever and 1 day's drowsiness and headache. Thirty years previously she had had pleurisy with effusion. Otherwise there was nothing to suggest tuberculosis. X-ray examination (Fig. 16) showed collapse of the right lower and right middle lobes (portable film). A chest consultant decided that the probable diagnosis was bronchogenic carcinoma with brain metastases. Bronchoscopy, however, disclosed a nodular lesion of the right stem bronchus with central necrosis. The gross appearance was consistent with carcinoma. The biopsy diagnosis was acute and chronic inflammation, with necrosis and possible tuberculosis. The sputum subsequently was positive for tuberculosis. Two years later the patient was making a slow but constant improvement on medical management.

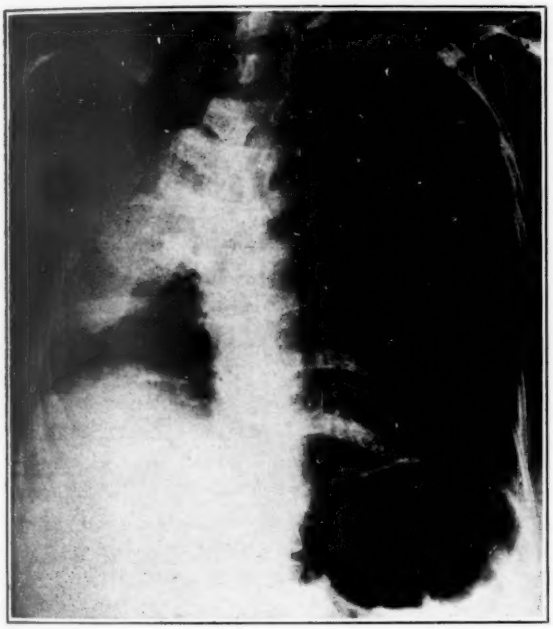


Figure 17. *Case 13.*

Upper right thoracoplasty, followed by persistent cough, positive sputum and wheeze; bronchoscopic examination, multiple tubercles in right main and right stem bronchi; later, complete stenosis.

This case is the reverse of Case 11, as here the probable clinical diagnosis was carcinoma, but bronchoscopy showed tuberculosis.

Case 13. J. G. (M. G. H. U153402), a 46-year-old woman, gave a history of right phrenicectomy for tuberculosis 2 years before entry. One year previously she had undergone a two-stage thoracoplasty, followed by persistent cough, positive sputum and wheeze. X-ray examination (Fig. 17) showed an upper right seven-rib thoracoplasty. Because of persistent cough, positive sputum and wheeze, bronchoscopy was performed, disclosing the right-upper-lobe orifice collapsed and the right main and stem bronchi studded with tubercles. Two months later bronchoscopy was repeated and the process was found to be more advanced, with stenosis of the right stem bronchus and involvement of the left main bronchus. Two years later on a medical regimen there was still moderate cough but less wheeze, and some slow improvement.

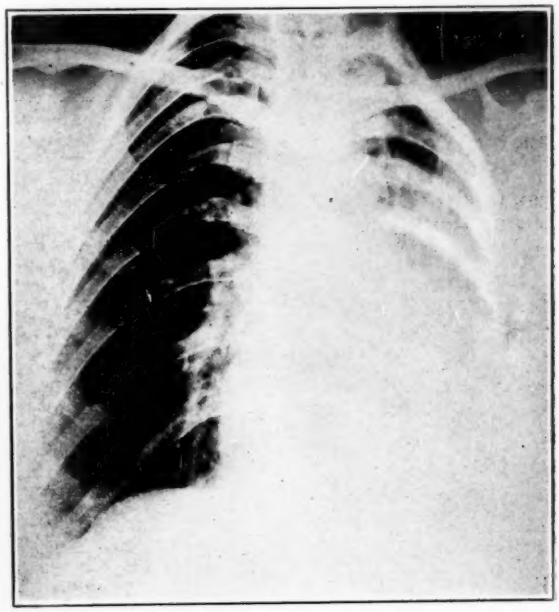


Figure 18. *Case 14.*

Fibrosis and calcification of left lung, following first-stage thoracoplasty for tuberculosis; persisting positive sputum; bronchoscopic examination, tuberculous stricture of left main bronchus; later, successful pneumonectomy.

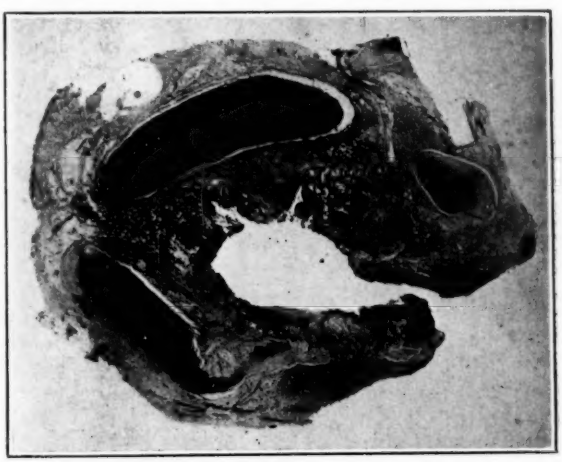


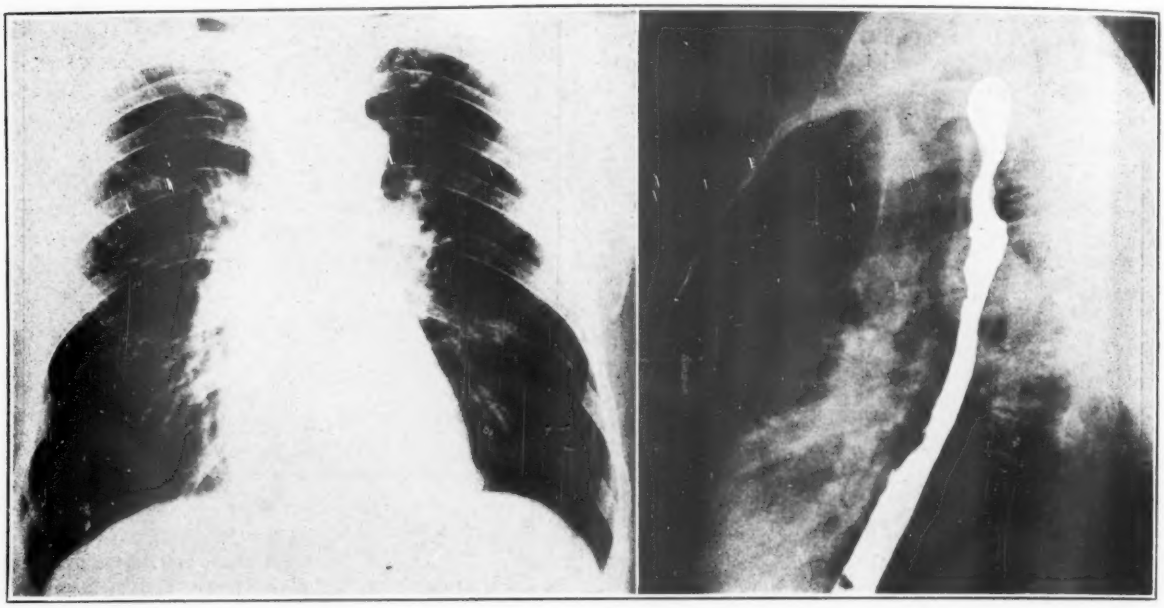
Figure 19. *Case 14.*

Low-power cross section of bronchus, showing markedly reduced lumen.

Bronchoscopy in this case demonstrated the presence of active tracheobronchial tuberculosis following thoracoplasty.

CASE 14. H. V. (M. G. H. U295413), a 42-year-old woman, entered the hospital complaining of left-sided wheeze and positive sputum associated with pulmonary tuberculosis of the left lung. Bronchoscopy prior to entry had shown an ulcer of the left main bronchus. Bronchoscopy showed narrowing of the left main bronchus in the region of the left-upper-lobe orifice. There was no evidence of activity. The appearance was that of a healed bronchial ulcer. A first-stage thoracoplasty was undertaken, followed by persistent wheeze. A second bronchoscopy, 6 months later, revealed a stricture of the left main bronchus just above the left upper lobe. The positive sputum persisted. X-ray examination (Fig. 18) showed fibrosis and calcification. A third bronchoscopy, 5 months later, again demonstrated stricture of the left main bronchus 2 cm. below the carina. There was no ulceration, and the lumen was only 3 cm. in diameter. Pneumonectomy was therefore performed by Dr. Churchill. The postoperative course was satisfactory and 3 months later the patient was reported as doing well. The reduced lumen of the left main bronchus is shown in a low-power cross section in Figure 19.

CASE 15. A. J. P. (M. G. H. U328726), a 38-year-old man, entered the hospital complaining of cough of 13 months' duration, hoarseness for 11 months and dysphagia for 5 weeks. Mirror laryngoscopy showed the left vocal cord to be paralyzed in the midline. X-ray examination (Fig. 20A) revealed a mass in the upper mediastinum, with narrowing of the esophagus and apparent destruction of the esophageal mucosa (Fig. 20B). The presumptive diagnosis was carcinoma of the esophagus, with involvement of the recurrent laryngeal nerve and invasion of the tracheobronchial tree. Esophagoscopy, however, showed a normal esophageal mucosa with evidence of extrinsic pressure. Bronchoscopy revealed an extensive proliferative mass involving the left main bronchus, the carina and the right main bronchus. The tissue removed at the time of bronchoscopy was reported as showing evidence of tuberculosis.



A B

FIGURE 20. *Case 15.*

A—*Upper mediastinal mass in patient with cough, hoarseness and dysphagia.* B—*Apparent destruction of esophageal mucosa; presumptive diagnosis, carcinoma of esophagus; esophagoscopy, negative; bronchoscopic biopsy, bronchial tuberculosis.*

This is obviously a very unusual case, for several reasons. Paralysis of a vocal cord is common in malignancy but rare in tuberculosis. The dysphagia appeared to be the presenting symptom but was apparently overemphasized, for the cough and hoarseness preceded it. However, most of the clinicians concluded that there was a probable malignancy of the esophagus. Bronchoscopy and esophagoscopy demonstrated the true nature of the process.

CONCLUSIONS

Among the most frequent causes of bronchial obstruction are carcinoma, benign tumor and tuberculosis.

The clinical picture may lead to an erroneous presumptive diagnosis, for the underlying cause of the obstruction frequently cannot be determined by laboratory and x-ray studies.

Bronchoscopy with biopsy or smear is necessary to establish a positive diagnosis.

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THE USE OF SULFADIAZINE IN THE MANAGEMENT OF SIMPLE MASTOIDECTOMY WOUNDS

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BOSTON

IN SEPTEMBER, 1941, Livingston,[1] of Chicago, reported a series of 13 cases in which sulfonamide drugs were used locally in mastoid cavities, the wounds being closed without drainage. The results were remarkable in that the postoperative course was greatly shortened. Apparently, this was the first report of the local use of sulfonamide drugs in mastoidectomy wounds, although they had previously been used in the treatment of compound fractures and peritonitis, as is well known.

The primary closure of mastoidectomy wounds without drainage was not new. Near the turn of the century it was a common practice among reputable otologists to close the wound after it had been allowed to fill with a blood clot — the so-called "blood-clot method." Sprague[2] and Reik,[3] among others, reported considerable success. They described how the blood clot became organized and filled in by the growth of fibroblasts and osteoblasts. This method fell into disuse, however, because it was quite unsuccessful in the hands of many surgeons; the clot frequently broke down, and the wound opened and subsequently healed by the slow process of granulation. Nevertheless, otologists were influenced to the extent that, instead of packing the mastoid wounds wide open, a method was devised whereby a drain was inserted in the cavity and the wound closed except at the site of the drain. This procedure has been generally employed up to the present day.

From the results of Livingston's report, however, one might assume that local chemotherapy would exert a sufficient bacteriostatic or bactericidal effect to make a primary closure feasible in a high percentage of cases. Yet there remained a reasonable doubt concerning the validity of his results, since these cases, as reported, were not controlled.

With this latter point in mind, we studied a series of controlled cases in which operation was performed at the Children's Hospital from October, 1941, through June, 1942. The present report is a summary of observations from these cases.

All cases were those in which the present illness was six weeks or under in duration and in which no sulfonamides had been given before hospital admission. The period of six weeks was a purely arbitrary one which, for the purpose of simplicity, we called the stage of acute mastoiditis. The series was then divided into three parts. Group A comprised those cases in which sulfadiazine‡ was placed directly in the mastoid wound at the close of operation and the wound was sutured without drainage. No sulfonamides were given by mouth. The Group B cases received sulfadiazine by mouth, both preoperatively and postoperatively, and the wound was sutured without drainage, no sulfadiazine being given locally. The Group C cases received no sulfonamide, either by mouth or within the wound, which wound was drained at the lower pole by a small wick of gutta-percha gauze.§

These cases were taken in rotation, Case 1 being placed in Group A, Case 2 in Group B, Case 3 in Group C, Case 4 in Group A, and so on. With the series controlled in this fashion, we hoped to rule out certain errors. First, the year-to-year variation in the severity of acute mastoiditis and its sequelae would be obviated. Secondly, there was a strong possibility that the level of sulfadiazine in the blood stream might be a factor in rapid healing. Sulfadiazine levels, in those who received sulfadiazine by wound only, showed values as high as 15 mg. per 100 cc. of whole blood, although in most cases the level was 1 mg. per 100 cc. or less. The level five days postoperatively was usually less than 1 mg. per 100 cc.

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‡The sulfadiazine used in this series was kindly supplied by the Lederle Laboratories, Pearl River, New York.

§Another group is readily apparent for its control value, that in which the wound is closed without drainage and without sulfonamides. This procedure was not undertaken, since we did not believe that it would prove to be of sufficient value to subject the patient to the necessary risk.

Technic

Group A

A complete simple mastoidectomy was performed in each case in Group A. Care was taken to enlarge the aditus ad antrum, so that in most cases the short process of the incus was exposed. In some cases this was obscured by granulation tissue. After the mastoid bone had been exenterated, the cavity was flushed with warm physiologic saline solution. A piece of gauze dampened with a 1:1000 solution of epinephrine was then placed in the cavity and interrupted periosteal sutures were taken with No. 0 or 00 plain catgut, but not tied. The pack was then removed and sulfadiazine powder was poured into the cavity from a sterile test tube. The periosteal sutures were tied. No attempt was made to pack the light, fluffy powder into the cavity. Some of the powder was dusted freely into the subcutaneous regions and along the skin edges. The skin was then closed with interrupted black-silk sutures, using the Poole mattress stitch. No pack was placed within the external auditory canal. From 0.5 to 2.0 gm. of sulfadiazine was used in each case, depending on the size of the cavity. The sulfadiazine had been previously autoclaved in cotton-stoppered test tubes at 270°F. for ten minutes. The adenoids were removed following mastoidectomy whenever they were found to be hypertrophied by palpation, roentgen examination or nasopharyngoscopy. Dressings were usually done on the second postoperative day, at which time it was possible to replace the bulky dressing applied at operation with a small postaural piece of gauze. Sutures were removed on the sixth to the eighth postoperative day. The ear canal was kept free of discharge by wiping with dry cotton swabs every four hours as long as needed.

Group B

A similar operation with closure was performed in Group B, the chief difference being that the sulfadiazine was not used locally, but instead was given by mouth for one day preoperatively and for seven to ten days postoperatively, in amounts sufficient to produce a blood level of 10 to 15 mg. per 100 cc. Postoperative dressings were essentially the same.

Group C

The operation in Group C was similar to that in Groups A and B. The wound was closed as in the first two groups, except at the inferior pole, where a gutta-percha gauze wick was inserted, extending up to the antrum. This wick was replaced on the second postoperative day by a small piece of rubber tissue, which was removed and reinserted every other day until drainage was minimal, at which time the wound edges at the lower pole were allowed to seal over.

Analysis of Results

Group A

The number of patients in Group A, in which sulfadiazine was used locally and the wound was sutured, was 16 and the number of cases of mastoiditis operated on 22, there being 6 cases of bilateral mastoidectomy. Of these 6, 2 cases deserve special mention. In one, the wound was closed on the right with sulfadiazine and drained on the left without sulfadiazine. The results here were entirely opposite from the remainder of the series, in that the drained ear ceased to discharge on the ninth postoperative day and the wound was healed on the seventeenth postoperative day, whereas the undrained ear discharged for thirty-three days. In another case, treated similarly, the undrained side healed in eight days, the drained side in twenty-four days.

In all, twenty operations were performed in which sulfadiazine was placed within the wound. All the wounds healed per primam. There were no complications, with the exception of one case that developed a subcutaneous postaural abscess on the eighteenth postoperative day, necessitating incision and drainage, with healing complete four days later. These cases, along with the other two groups, are summarized in Table 1.

Bacteriologic findings. Sixteen wounds showed beta-hemolytic streptococcus in pure culture, 1 showed beta-hemolytic streptococcus and *Staphylococcus aureus, and 1 Haemophilus influenzae.* The cultures from 2 wounds showed no growth.

Pathologic changes. All removed tissue revealed pus, granulations or necrosis, alone or in combination. One case had a large subperiosteal abscess, which extended up to the temporal region, causing trismus.

Age. The children varied from nine months to six years and eleven months in age.

Follow-up. This was carried out on every patient and varied from three weeks to six months. One patient developed a postaural abscess after six months, which healed without event. This was the only recurrence of mastoid-cavity infection.

Hospitalization and drainage. The average length of aural drainage was 10.0 days. The average length of time required for both the wound and middle ear to heal, including complications, was 10.1 days.

Group B

The number of patients in Group B, in which sulfadiazine was given by mouth and the wound

was closed, was 15, and the number of operations for mastoiditis 18. Of these, 1 patient had a bilateral mastoidectomy in which the right wound was sutured and the left was drained. Both ears ceased to discharge in six days. The right wound healed per primam. The left healed entirely except at the drain site, where final healing occurred on the fifteenth postoperative day.

In all, 17 mastoid processes were operated on by this method. Of these, 15 healed per primam. One developed a subcutaneous wound infection on the fifth day, which healed by the tenth day. In another case, a bilateral mastoidectomy, the left postaural wound broke down and had to be resutured. Final healing took place on the twentieth postoperative day. Two cases had small stitch abscesses.

Bacteriologic findings. Cultures from the mastoid processes showed beta-hemolytic streptococcus in 5 wounds, pneumococcus (not typed) in 1, gram-positive rods (not identified in 1), and no growth in 10. This is a large number of negative cultures, explained perhaps by the fact that sulfadiazine was given by mouth preoperatively. The ears on admission showed a much greater number of positive cultures for pathogenic organisms, only 3 being nonpathogenic.

Pathologic changes. All removed tissue revealed pus, granulations or necrosis, alone or in combination. In one case there was a definite perisinus abscess, and in another granulations were present on the sinus. One case developed a subperiosteal abscess.

Age. The children varied from ten months to eight years and eight months in age.

Follow-up. This varied from one week to four months. There was no recurrence of ear infection.

Hospitalization and drainage. The average length of aural drainage was 8.2 days. The average of the time for both the wound and middle ear to heal, including complications, was 9.0 days.

TABLE 1. *Data on the Three Groups of Patients.*

DATUM	GROUP A	GROUP B	GROUP C
Number of patients	16	15	15
Number of ears operated on	20	17	16
Age incidence	9 mo. to 6 yr. 11 mo.	10 mo. to 8 yr. 8 mo.	5 mo. to 6 yr. 4 mo.
Wound healing	Per primam	Per primam except for 2 cases	Healing complete in 3 wk. (11 cases)
Average days of aural discharge	10.0	8.2	Over 15 days
Bacteriology (operative wound culture)	16, beta-hemolytic streptococcus; 1, beta-hemolytic streptococcus and *Staph. aureus*; 1, *H. influenzae*; 2, no growth.	5, beta-hemolytic streptococcus; 1, pneumococcus; 1, gram-positive rods; 10, no growth.	10, beta-hemolytic streptococcus; 1, beta-hemolytic streptococcus and *Staph. aureus*; 1, pneumococcus; 4, no growth.
Complications	1, subcutaneous postaural abscess on 18th postoperative day	1, wound broke down, 1, wound became infected; 2, wound developed stitch abscess	1, subcutaneous wound infection, with healing by secondary intention; 1, cavity revised after 4 wk.; 4, cavity revised after 7 wk.
Average days of hospitalization	10.1	9.0	Over 21

Group C

The number of patients in Group C, in which no sulfadiazine was given and the wound was drained, was 15, and the number of mastoid processes operated on 16. Of these patients, 10 had an uneventful convalescence. In 1 case, the wound edges separated and healed by secondary intention. In 4 cases, the mastoid cavities were revised after five to seven weeks of drainage.

Bacteriologic findings. Of the cultures from mastoid wounds, 10 showed beta-hemolytic streptococcus, 1 showed beta-hemolytic streptococcus and *Staph. aureus,* 1 pneumococcus (not typed), and 4 no growth.

Pathologic changes. All removed tissue revealed pus, necrosis or granulations, alone or in combination. Two cases showed subperiosteal abscesses.

Age. These children varied from five months to five years and four months in age.

Follow-up. This ranged from one week to six months. Two cases showed recurrent aural discharge, 1 as a result of measles. Both cases healed uneventfully. One case was reoperated on after five weeks and 3 after seven weeks of continued wound or ear drainage. Ordinarily, these might have been allowed to drain considerably longer. It is interesting to note that 3 patients were infants under one year of age with poor nutrition.

Sulfadiazine was used at the second operation, with prompt healing, in 3 of the 4 reoperated cases.

Hospitalization and drainage. The length of time of aural discharge averaged 15 days, and wound healing averaged 3 weeks, except for the 4 cases that were revised. In these, the convalescence was considerably prolonged.

Discussion

On final analysis, the results obtained in this series of mastoidectomies seem to be significant. Although the number of cases in each group is quite small, the startling differences in the postoperative courses at least warrant further study. Study of postoperative audiograms would be of considerable interest in the final evaluation of our results, but this was not particularly feasible since all the patients were children. However, it was our impression that the hearing was not altered appreciably in those with sulfonamide therapy, since these children have had, after six weeks at the most, normal tympanic membranes and no marked loss of hearing by cursory examination.

The choice of any one of the sulfonamides in preference to others is still an open question. Sulfanilamide has been advocated for use locally because of its high solubility. However, the solubility seems to be relatively unimportant, provided that the opening into the middle ear is enlarged. In this way, the cavity decompresses itself. In most of our cases, we recovered sulfadiazine crystals suspended in the serous aural discharge. Perhaps the lesser soluble substance has a more prolonged local action. It is the opinion of one of us (C. A. T.) that a combination of sulfanilamide and sulfadiazine placed within the wound, with small amounts of sulfadiazine given by mouth postoperatively, may be the method of choice. The specificity of the sulfonamide drug used locally probably does not enter into the picture, since, at the concentrations developed locally, all these drugs have a broad bacteriostatic coverage.

Postoperative ear cultures obtained in some of the cases in Groups A and B often showed the offending organism to be present until the ear ceased to discharge. In 2 cases, it was necessary to permit the escape of serum, which had collected beneath the wound. These cases showed a minimal amount of aural discharge, indicating a block, probably in the region of the aditus.

The method of wound closure is still an open question. Guerry and Putney[4] have reported a series of controlled cases in which a sulfathiazole gauze pack was used. Their results, too, showed a remarkable improvement in postoperative convalescence.

In our series, those who received the sulfonamide by mouth did about as well as those who received it locally. The major difference, however, was in wound healing, which was definitely improved when sulfadiazine was used locally.

Summary and Conclusions

A controlled series of 41 cases of simple mastoidectomy is presented, divided into three sets as follows: Group A, those receiving sulfadiazine locally, the wound being closed without drainage; Group B, those receiving sulfadiazine by mouth, the wound being closed without drainage; and Group C, those not receiving sulfadiazine, the wound being drained in the usual fashion.

The hospitalization required in Groups A and B averaged around ten days, the wounds healing per primam and the tympanic membrane being healed and dry at that time. The wound broke down, in only 1 case, in Group B. There were no untoward results. The patients in Group C had the usual prolonged convalescence.

At this time, we cannot advocate with impunity any one method for the control of wounds in mastoidectomy, although sulfonamide therapy seems to be of definite value. Certainly the prime requisite for good results is the performance of a standardized, thorough, simple mastoidectomy.

This report, based on relatively few cases, is presented for the objective data that it contains. When it is taken together with other similar reports, which will undoubtedly appear in the literature, the correct procedure for the control of mastoidectomy wounds will eventually arise.

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CHRONIC MILIARY TUBERCULOSIS

Report of a Case

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BOSTON

IN 1937, Hoyle and Vaizey[1] published their monograph on chronic miliary tuberculosis, presenting 120 cases collected from the literature and from their own experience. Since the publication of their book, several additional cases have been reported. These reports have served to demonstrate the benign course that may be followed by a disease that only recently was considered to be invariably fatal.

AGE INCIDENCE

Chronic miliary tuberculosis has been recorded at almost all ages, from the first to the seventieth year of life. The majority of cases occur in the second, third or fourth decade. Distribution between the sexes is approximately equal. An insignificant number of patients give a history of tuberculosis. Other previous illnesses and family histories of tuberculosis have a questionable influence on the incidence.

SYMPTOMS AND SIGNS

In most cases the onset is insidious, with slight symptoms and signs. Cough, expectoration and dyspnea are the commonest pulmonary symptoms, and these are usually mild. In some cases a cold dates the onset of the disease. Loss of weight and weakness are frequent constitutional complaints. Symptoms of extrapulmonary tuberculosis first bring some cases under observation.

The physical signs are inconstant. Slightly over half the cases present wasting and fever, the latter usually of mild degree. The commonest abnormal physical signs are those in the lungs, but even these are absent in one fifth of the cases. The pulmonary findings vary from localized evidence of infiltration to signs of generalized pulmonary involvement. Of the extrapulmonary signs, splenic enlargement and lymphadenopathy predominate. A small number of cases present evidence of tuberculosis of the bones or joints.

RADIOLOGIC FINDINGS

The only constant objective finding of chronic miliary tuberculosis is the typical appearance of the pulmonary lesions in roentgenograms of the chest. In all except a few cases the distribution is bilateral, with total pulmonary involvement. In addition to the usual small, soft, ill-defined lesions, occasional larger areas of infiltration or excavation are seen. The roentgenographic picture is in most cases indistinguishable from that of acute miliary tuberculosis.

Sayé[2] has described a nonapparent form of chronic miliary tuberculosis, which he detected in over 5 per cent of students examined radiologically at the University of Barcelona. These cases exhibited fine linear and nodular shadows in the lung fields. The significance of the lesions was to be determined by subsequent examinations. As yet no confirmatory series of similar cases has been reported elsewhere.

LABORATORY DATA

A bacteriologic diagnosis can be established in about half of all cases, and a histologic diagnosis in an additional small percentage (15 to 20 per cent) during life. Necropsy establishes the diagnosis in another 10 per cent, although even here the tubercle bacillus is often not demonstrated. Altogether, there remain about one fifth of all cases without bacteriologic or histologic evidence to support the diagnosis. In this group, the symptoms, physical signs, typical roentgenographic findings and clinical course warrant the diagnosis.

The tuberculin test has been reported in only a few cases, and in some has been negative. The failure to find the tubercle bacillus and the presence of a negative tuberculin test, even where the histologic findings are consistent with tuberculosis, leave room for doubt concerning the accuracy of the diagnosis. The close resemblance of chronic miliary tuberculosis to Boeck's disease has undoubtedly led to the improper classification of many cases.

CLINICAL COURSE

Where to draw the line between acute and chronic miliary tuberculosis is difficult to decide. Hoyle and Vaizey[1] considered that chronic cases should present a clinical course of at least three months. They found that of 64 patients sufficiently observed, 13 died within six months, 33 died within eight years (with an average length of life of two years from the date of onset of symptoms), and 18 lived to be considered arrested cases. In

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those who died, tuberculous meningitis and acute generalized tuberculosis were the leading causes of death. In those who lived to be followed by serial roentgenograms, the lesions appeared stationary in some, became more discrete or calcified in others, and actually disappeared in a few. The reported cases have been too few to offer reliable criteria for predicting the course of the individual patient.

Morbid Anatomy

In those cases that have come to autopsy, the pulmonary lesions have been most constant. Except in cases terminating with an acute generalized spread of the disease, extrapulmonary lesions have not been frequent. In the lungs, numerous evenly distributed, tiny, gray or white, fibrous miliary foci, sometimes calcified, appear. Rarely are the lesions more than a few millimeters in diameter. Histologically the lesions are characterized by a great amount of fibrous tissue and by scant cellular infiltration in which giant cells and epithelioid cells predominate. Caseation has been unusual.

There has been much argument about the mode of spread of this disease. It is conceivable that a tuberculous lesion erodes the thoracic duct or a blood vessel and discharges tubercle bacilli into the blood stream. Whether a generalized systemic distribution of lesions or a restricted pulmonary distribution occurs depends on whether the channel involved is a part of the greater or lesser circulatory system. This concept of a hematogenous route of dissemination has met with greater popularity than that of a lymphogenous one. That the latter may occur, however, has been well demonstrated by Hoyle and Vaizey in the pathologic findings in one of their cases. The possibility of a bronchiogenic mode of spread must also be recognized, although a uniform dissemination of lesions throughout both lungs by this route would hardly be expected.

Diagnosis

The more usual conditions offering difficulty in the differential diagnosis of chronic miliary tuberculosis are Boeck's disease, generalized carcinomatosis, pneumoconiosis and pulmonary congestion. The exclusion of rare conditions such as fungus infections, periarteritis nodosa and Hodgkin's disease may also present difficulty.

Boeck's disease is often hard to exclude. So closely alike may it and chronic miliary tuberculosis appear, that some clinicians believe both terms to refer to the same disease. A negative tuberculin test, the absence of tubercle bacilli and the presence of characteristic bone lesions in the phalanges are points in favor of the diagnosis of Boeck's disease. Even at necropsy it is often difficult to differentiate these conditions. Snapper and Pompen[3] consider that the absence of tubercle bacilli and of caseation distinguishes Boeck's disease from chronic miliary tuberculosis.

Generalized carcinomatosis may be differentiated by extreme dyspnea, the absence of tubercle bacilli and a rapidly fatal course. There is often an additional history of pain in one or more bones, leading to the discovery of other metastases.

Pneumoconiosis is excluded by the absence of a history of dust exposure.

In pulmonary congestion the preponderance of the opacities and physical signs about the hili and bases of the lungs should serve to indicate this diagnosis. An abnormal size or shape of the heart would also be suggestive.

Proof of the diagnosis of chronic miliary tuberculosis rests, during life, on finding the tubercle bacillus; after death, on finding the characteristic histologic lesions. The bacilli may be found in the sputum or in the extrapulmonary lesions. In a number of cases neither a bacteriologic nor a histologic diagnosis is possible and it becomes necessary to rely on serial roentgenography and the clinical aspects of the case. In the case reported below the diagnosis rested on these two factors alone from 1939 to 1942, when the patient developed a cavity and a positive sputum. The presence of pericarditis with effusion at one time in the course of the disease lent additional weight to the probability of a miliary tuberculous process. No case of chronic miliary tuberculosis with pericardial effusion has, to my knowledge, been recorded before.

Treatment

As in all degrees of pulmonary tuberculosis, treatment consists of rest and general hygienic and nutritional care. In a few cases with localized areas of infiltration or excavation, unilateral pneumothorax has been successful in controlling the disease. Partial bilateral pneumothorax has been recommended, but remains untried. Sayé[2] thought that some of his patients were benefited by injections of Sanocrysin.

Case Report

A. S., a 58-year-old Greek tanner, was admitted to the Middlesex County Sanatorium on July 26, 1939. The past history was irrelevant. There was no history of contact with tuberculosis or exposure to silica-containing dust.

The patient was well until 4 or 5 years before admission, when he first experienced dyspnea on exertion and slight swelling of the ankles in the afternoon. Easy fatigability was sufficient to necessitate stopping work. Intermittent aching in the right side of the chest and a slight cough began at that time, and he began to raise an ounce of thick yellow sputum per day.

The patient tolerated these symptoms, however, and it was not until 15 months before admission that he consulted a physician. At that time his chief complaint was a burning postprandial epigastric pain. He was admitted to another hospital, where a diagnosis of chronic gastritis, acute cardiac decompensation and miliary tuberculosis was made. A roentgenogram taken on April 20, 1938 (Fig. 1), showed scattered mottled infiltration throughout both lung fields and thickening of the interlobar septum on the right. The lower two thirds of the left lung was obscured by an enormous cardiac shadow extending from the left axilla to a point 5 cm. beyond the right pulmonary hilus. The patient was discharged after 3 weeks.

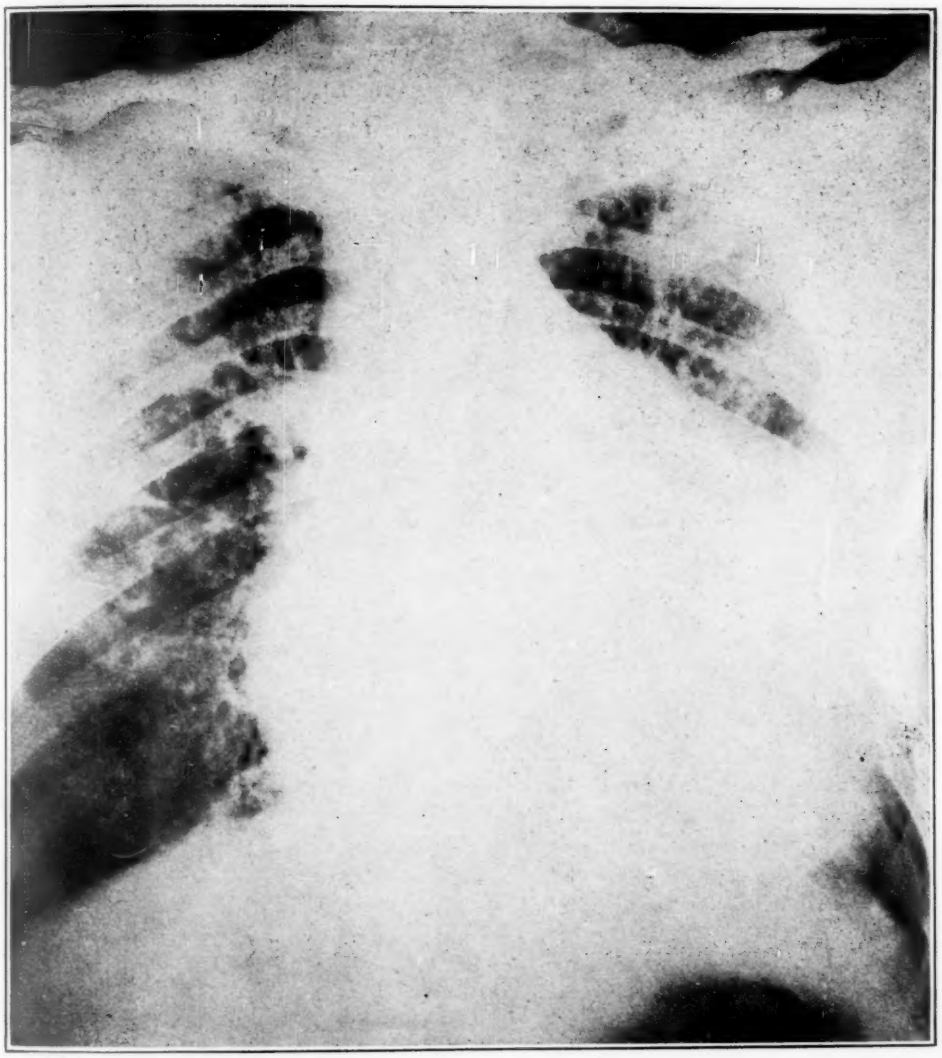

FIGURE 1.

The patient returned to the hospital 7 months later. A roentgenogram on December 9 showed a marked decrease in the size of the cardiac shadow, which was then normal. The right lung showed no change. On the left there was a pleural reaction casting a haze over the entire lung. The tubercle bacillus was not found.

The patient was not heard from again until June 5, 1939, when he came to the Diagnostic Clinic. His chief complaint was, as before, a burning pain in the epigastrium. A roentgenogram showed slight clearing of the pleural reaction on the left. He re-entered the hospital July 26. There had been no increase of dyspnea, fatigue, swelling of the ankles, cough or expectoration.

Physical examination revealed a well-developed, slightly undernourished, tired-looking man. The skin was clear. There were a few small, firm, lymph nodes palpable in the neck and in both axillas. Examination of the ears, eyes, nose and throat revealed no abnormality. The optic fundi were clear. The chest was slightly barrel-shaped, and expansion was equal on both sides. The lungs were resonant, and the breath sounds vesicular throughout. At the right base posteriorly there was a faint friction rub. A few posttussic medium rales were heard at the left apex posteriorly and in the first left interspace. The heart was of normal size, with a regular rhythm and no murmurs. There was slight sclerosis of the peripheral arteries. The blood pressure was 130/80. The liver and spleen were not felt. The remainder of the examination was negative. Fluoroscopy revealed normal excursion of the diaphragm on each side. The heart was of normal size and contour.

The cardiac outline was indistinct, with a regular beat of fair quality. A roentgenogram of the chest, taken on July 27 (Fig. 2), showed no change.

The red-cell count was 3,900,000, and the hemoglobin 70 per cent (Sahli). The urine was negative, and there was no blood in the stool.

The patient remained in the hospital for 102 days. The temperature, pulse and respirations remained normal. He raised about 30 cc. of semithick, nonodorous, yellowish sputum daily, which was negative for fungi, and for tubercle bacilli even after inoculation of a guinea pig. He was treated by rest, a bland diet and Sippy powders, with relief of his pain, improvement in his general condition and a weight gain of 5 pounds. A subsequent red-cell count was normal. Fluoroscopy of the gastrointestinal tract after a barium meal and a plain film of the abdomen revealed no abnormality. X-ray films of the hands showed no evidence of Boeck's disease. The tuberculin test was positive. A roentgenogram of the chest in the following October showed no change.

A diagnosis of chronic miliary tuberculosis was made and the patient was discharged, to be followed in the Outpatient Department. At periodic check-ups he complained of abdominal cramps, occasional diarrhea, cough and expectoration. His general condition appeared unchanged, as did the roentgenograms of the chest, through September, 1941. The sputum remained negative for tubercle bacilli.

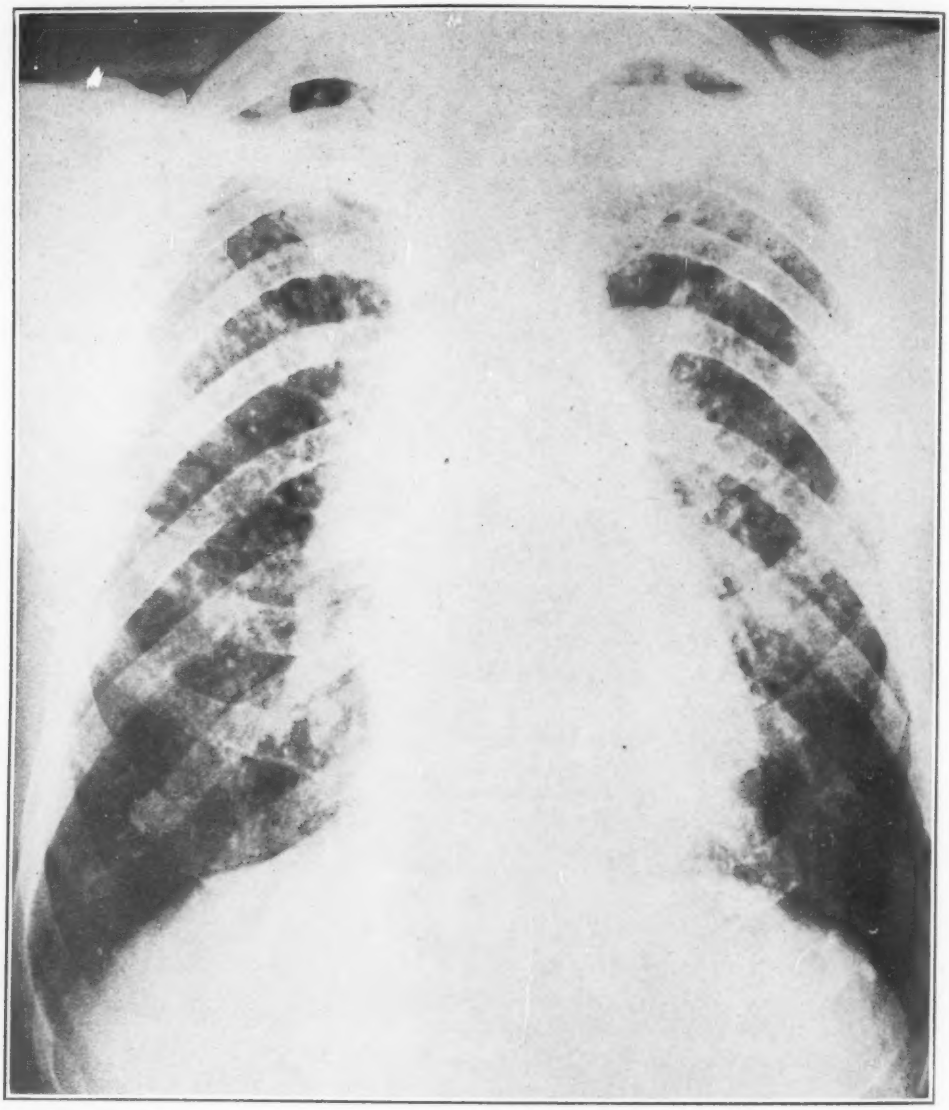

FIGURE 2.

The patient was readmitted May 4, 1942, because of recent slight hemoptysis. Some edema of the lower extremities of a few weeks' duration was present. He had been taking digitalis for 5 months. Physical examination revealed fair nutrition, slight cyanosis of the lips and nail beds and frequent coughing productive of small amounts of yellowish sputum. No lymph nodes were palpable. The trachea was in the midline. There was slight dullness over the right side of the chest but no rales. On the left there was similar dullness, but coarse moist rales were heard over the upper half. The heart did not appear to be enlarged, and was regular except for occa-

sional extra beats; no murmurs were audible. The pulse was 80, the respirations 20, and the blood pressure 140/70. There was no orthopnea. The liver and spleen were not palpable. There was slight edema of the extremities.

Repeated sputum specimens were positive for tubercle bacilli on direct smear. The tuberculin test was positive. The red-cell count was 4,200,000, with 90 per cent hemoglobin (Sahli), and the white-cell count was 8500, with a normal differential count. A blood Hinton test was negative. The urine was normal. A roentgenogram showed cavitation of the upper half of the left lung. The distribution of the miliary lesions seen previously remained unchanged, with some increase in the reaction around the lesions on the left. The cardiac silhouette remained unchanged.

At present the patient is on bed rest. Fever was present up to 100.0°F. during the first 2 weeks after discharge, since when it has been normal except for an occasional rise to 99.0°F.

Although it is appreciated that the recovery of tubercle bacilli from the sputum of this patient does not prove the diagnosis of chronic miliary tuberculosis, the clinical course of the disease makes such a diagnosis extremely likely.

Summary

A probable case of chronic miliary tuberculosis is presented, with a review of the outstanding features of this disease.

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MEDICAL PROGRESS

THE SULFONAMIDES*

II. Their Clinical Use

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BOSTON

IN the first section of this report[1] the basic knowledge about the sulfonamides was reviewed. It was pointed out that their activity depends on an inhibition of the multiplication of virulent bacteria in the tissues, and that this bacteriostatic activity can be nullified specifically by para-aminobenzoic acid in vitro and by pus and necrotic tissue in vivo. The essential facts about the pharmacology of this group of drugs were presented. With this material as a basis, the second section will be devoted to the use of the sulfonamide drugs in clinical practice.‡

In order to make this presentation as useful as possible, I have organized it in the form of answers to a series of questions which constantly ecur in the practice of medicine. These answers may seem too dogmatic to some, too general to others. They are far from perfect, but represent the principles worked out from clinical experience and from discussions with others interested in the field. Without committing any of my colleagues to agreeing with me, I should like to admit my debt to the following, from whose ideas and criticisms most of these principles have evolved: Dr. Paul B. Beeson, Dr. John Dingle, Dr. Maxwell Finland, Dr. Chester S. Keefer, Dr. Perrin Long, Dr. Champ Lyons, Dr. J. A. V. Davies and Dr. W. B. Wood, Jr.

I. What are the indications and contraindications for the use of the sulfonamides?

Because of the brilliant therapeutic results achieved with these drugs, there has been an increasing tendency on the part of physicians to administer them to any patient with a fever. If they were harmless drugs, this would merely be intellectually indefensible, but since they are not only powerful but potentially dangerous remedies, it is as wrong to give them without specific indications as it is to deprive a patient of their benefits when he is seriously ill.

Indications

Adequate Therapy

Infections due to susceptible organisms should be treated with sulfonamides *only if they are severe or spreading*, because it is only under these circumstances that these drugs are very effective. Thus, a physician should know the etiology of common infections and possess sufficient clinical judgment to realize when an infection is spread-

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‡In this presentation, the local application of these drugs will not be considered, since this is a strictly surgical problem in which I am neither experienced nor competent.

ing and menacing his patient. In a review published several years ago, I[2] tabulated the factors which influence the efficacy of sulfonamide therapy, and these still hold true. The drugs are most effective in combating rapidly spreading infections, when the organisms are growing in a serous type of exudate free of sulfonamide inhibitor and when fever is high, as elevated temperature not only decreases the rate of multiplication of certain bacteria, but markedly increases the bacteriostatic efficiency of the sulfonamides.[3] Furthermore, immunity on the part of the patient greatly enhances the therapeutic response. On the other hand, where there is little fever, and particularly when there is tissue necrosis, the sulfonamides have little effect on the lesion except with a highly susceptible organism such as the gonococcus. The following case illustrates some of these points.

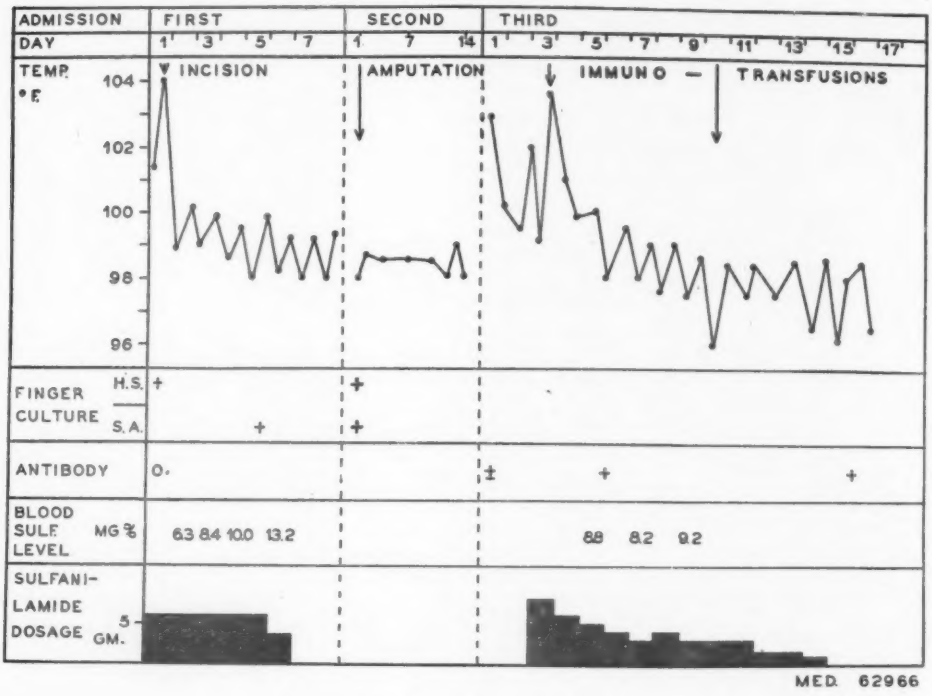

FIGURE 1. *Clinical Course of Case 1.*

CASE 1 (P.B.B.H. S62639, S62778 and S62966) (Fig. 1). The patient, a surgeon, punctured his finger while operating on a man with a hemolytic streptococcus septicemia. Twelve hours later he developed throbbing pain in the finger and had a shaking chill. On admission, high fever, swelling and tenderness of the finger and lymphangitis extending up to the shoulder were observed. The finger was incised, and a Group A hemolytic streptococcus isolated from the serosanguineous fluid was obtained. On moderate doses of sulfanilamide, heat and rest, there was a prompt fall in temperature. Because of the rapid improvement and the marked anorexia and subjective discomfort experienced from the drug, its administration was discontinued on the 6th day. Cultures taken from the finger when another incision was made on the 5th day because of continuing tenderness, showed only *Staphylococcus aureus*. Phagocytosis of the hemolytic streptococcus isolated from the finger by the patient's own defibrinated blood was nil (indicating no antibody). The patient was discharged on the 12th day to continue hot soaks to the finger, which still showed tenderness.

Four days later, on the 16th day of his illness, the patient was readmitted because of increasing pain, swelling and tenderness of the finger. X-ray films showed osteomyelitis of the 2nd and 5th phalanges. The 5th phalanx and the infected portion of the 2nd phalanx were amputated at operation, when small abscesses were opened on either side of the sheath of the flexor tendon. The pus contained both beta-hemolytic streptococcus and hemolytic *Staph. aureus*. Following operation, the finger healed well, and convalescence was uneventful. Swelling had completely subsided and there was only a small amount of serous drainage at one angle of the healing stump, when the patient was discharged on the 13th postoperative day.

For the next 8 days the patient made satisfactory progress, receiving physiotherapy for the stiffness of the finger and daily dry sterile dressings. Except for a reddish-blue color of the stump and a tendency for it to throb when dependent, the finger seemed to be doing well. On the 9th day after discharge and on the 38th day of illness, following a 40-minute walk in the cold through heavy snow, the patient developed chilly sensations, malaise, headache and lumbar backache. He was admitted for the third time with a temperature of 103°F. and a white-cell count of 16,900. The finger appeared normal on admission, and a tentative diagnosis of grippe was made. However, 36 hours after admission, the white-cell count was still elevated, the finger stump and adjacent areas of the hand became reddened, warm and tender, red streaks

appeared running up the arm to the axilla, and the lymph nodes of the axilla became tender and palpable. Consequently, sulfanilamide therapy was instituted, and because the patient's blood only showed a low titer of opsonins for the strain of hemolytic streptococcus from his finger, he was given 500 cc. of blood from a donor found to possess opsonins for this strain. With the combination of these measures and local heat and immobilization, the fever, lymphangitis and lymphadenitis subsided rapidly. He was given full doses of sulfanilamide for 3 days, then gradually decreasing doses, because of an adequate blood level (the fluid intake was poor) for the next 9 days. Following a second immunotransfusion, chemotherapy was discontinued and the patient had no further difficulties, except for some circulatory disturbances in the finger and a moderate anemia, which gradually disappeared.

Comment. This case demonstrates the efficacy of sulfanilamide in controlling the acute invasive manifestations of hemolytic streptococcus infection, as shown by the rapid subsidence of fever and lymphangitis on the 1st and 3rd admissions. However, the drug, despite adequate levels and early treatment, did not sterilize the local lesion, perhaps because of the accompanying staphylococcal infection and suppuration. The flare-up that occurred at the 3rd admission probably had its origin in a thrombophlebitis of one of the veins in the finger stump. Because the patient had had recurrences and did not tolerate sulfanilamide well, he was given antibody by transfusion from two donors whose blood contained opsonins for his organisms. Chemotherapy was then discontinued without further flare-up, but this might have occurred anyway. One must not underestimate the value of the time-honored surgical procedures of local heat and immobilization in the control of the lymphangitis, nor of amputation in removing the suppurating focus once localization occurred.

TABLE 1. *Infections Responding to Sulfonamide Therapy.*

TYPE OF INFECTION	DISEASE OR CAUSATIVE ORGANISM	DOSAGE	BEST DRUG†	ACCESSORY THERAPY
Local sepsis with spread (including tissue and wound infections); infections of ear, nose, and throat; osteomyelitis.	Hemolytic streptococcus (erysipelas, septic throat and so forth)	Regular*	S.D. (S.A.)	Heat, rest and immobilization; incision and drainage.
	Staph. aureus	Regular	S.T. (S.D.)	Heat, rest and immobilization; incision and drainage.
	Gas bacilli	Regular	S.T. (S.D.)	Antitoxin; x-ray.
Pneumonia and early empyema	Pneumococcus	Regular	S.D. (S.T.)	Antiserum in very severe cases
	Hemolytic streptococcus	Regular	S.D. (S.A.)	
	Staphylococcus	Regular	S.T. (S.D.)	
	Friedländer bacillus	Regular	S.T. (S.D.)	Antiserum, if available
Meningitis (lumbar puncture used only to relieve increased pressure and give information on progress)	Pneumococcus	Regular	S.D. (S.P.)	Intravenous rabbit antiserum
	Hemolytic streptococcus	Regular	S.D. (S.A.)	
	Meningococcus	Regular	S.D. (S.T.)	Intravenous antiserum rarely
	H. influenzae	Regular	S.D. (S.P.)	Intravenous rabbit antiserum
	Staph. aureus	Regular	S.T. (S.D.)	
Septicemia	Most organisms	Regular	S.D.	For *all* cases: transfusions; specific antiserum, when available; surgical removal of foci.
	Staph. aureus	Regular	S.T.	
	Gram-negative enteric bacilli	Regular	S.T. (S.D.)	
Venereal infections	Gonorrhea	2 gm. daily for 10 days	S.T. (S.D.)	Fever therapy in resistant cases
	Gonococcal arthritis	6 gm. daily	S.T. (S.D.)	Aspiration
	Lymphogranuloma venereum	Regular	S.T. (S.D.)	
	Chancroid (Ducrey bacillus)	Regular	S.T. (S.D.)	
Urinary infections	All organisms except enterococcus	2–4 gm. daily, unless septicemia present	S.T. (S.D.)	Surgery for calculi, obstruction and so forth
Miscellaneous infections	Actinomycosis	4 gm. daily for many months	S.D. (S.A.)	Rest; surgery.
	Trachoma	Small	S.P. (S.A.)	Local treatment
	Brucellosis	Regular	S.T. (S.A.)	Chemotherapy for acute attack (trial)
	Anthrax	Regular	S.T. (S.P.)	Antiserum
Peritonitis	Various organisms	Regular	S.D. (S.A.)	Surgery; plasma
Puerperal sepsis	Hemolytic streptococcus	Regular	S.D. (S.A.)	Transfusions
	Cl. welchii	Regular	S.D. (S.T.)	Antitoxin
	Mixed infection	Regular	S.D. (S.T.)	
Bacterial endocarditis	*Str. viridans* (salivary)	Regular or extra heavy	S.T. (S.D.)	Fever therapy; neoarsphenamine.
	Gonococcus or meningococcus	Regular or extra heavy	S.D. (S.T.)	Fever therapy

*Regular dosage = sufficient to maintain adequate level.
†S.A. = sulfanilamide; S.D. = sulfadiazine; S.T. = sulfathiazole; S.P. = sulfapyridine.

It cannot be emphasized too strongly that the effectiveness of sulfonamide therapy will always be limited to a considerable extent by the accuracy of

the bacteriological diagnosis. The treatment of serious infections is difficult when no such diagnosis has been made and when there is no bacteriological check on the progress of the patient. For that reason, before chemotherapy is instituted, cultures of the local lesion and the blood should be taken if possible, as has been customary with lobar-pneumonia patients before the institution of serum therapy. On the other hand, chemotherapy should never be deferred when it is clearly indicated solely because of a lack of laboratory facilities. Table 1 presents in compact form the types of infection in which the sulfonamides are known to be effective, the type of dosage required, the drug of choice and any accessory therapy that should be given.

There are a few infections which are relatively mild, but which menace the community by their infectiousness or the individual by their tendency to produce serious chronic disability. If such an infection is susceptible to sulfonamide therapy, these drugs are certainly indicated in order to prevent serious end results. In this group belong gonorrhea, trachoma, lymphogranuloma venereum and the majority of urinary-tract infections (Table 1). These are usually mild in their early phases, but potentially serious, and all respond to some degree to chemotherapy.

Three-day Trial of Therapy

If a patient is obviously seriously ill with an infectious disease and the physician cannot make a definite diagnosis, he has no right to withhold sulfonamide therapy. The treatment carries a risk of perhaps 0.2 per cent mortality in competent hands, which is too small to justify the denial of a form of therapy that has wide application to many types of infection, provided the patient is seriously ill. Under such circumstances a three-day trial of the sulfonamides is entirely justified. At the end of this period, a bacteriologic diagnosis may have been made, so that the physician will have some basis for a decision about further chemotherapy. If no response to adequate therapy occurs in three days, there is little sense in continuing a drug that has not influenced the course of the disease.

This situation arises most frequently in cases of puerperal infection. The mortality rate of puerperal sepsis due to hemolytic streptococci used to be about 25 per cent. With the prompt administration of the sulfonamides it has been brought to a very low figure. Every hour's delay in starting treatment seriously decreases the patient's chance of survival, and therefore sulfonamides should be administered as soon as a definite postpartum temperature rise above 101°F. occurs. At the same time cultures of the blood and uterine cavity should be taken. However, the vast majority of cases of puerperal sepsis are not caused by beta-hemolytic streptococci, but by organisms normally present in or near the genital tract, particularly colon bacilli and anaerobic streptococci. The latter do not respond to the sulfonamides; hence in most cases, after a three-day trial, fever and chills may still be present. By this time cultures should be available. If no organisms such as beta-hemolytic streptococci, virulent staphylococci or *Clostridium welchii* have been found, and adequate chemotherapy has not caused a marked reduction in temperature, it should be discontinued.

Prophylactic Therapy

Animal experimentation has demonstrated that the sulfonamides are frequently even more effective in the prevention of infection than in its cure. For this reason their use as prophylactic agents has frequently been advocated. This is a difficult subject on which to make rules, as the decision usually has to be made in the individual case. It is certain that if enough patients receive the sulfonamides prophylactically, someone is going to die from them. Thus, there is a definite though probably minute risk to life. That this really exists is attested by the death recently reported by Stowell and Button.[4] Beyond this there is the risk of sensitizing the patient, so that future sulfonamide therapy for more important reasons may produce severe reactions. Against these risks should be balanced the chances of infection and the dangers therefrom. The following are situations in which these drugs should probably be used prophylactically. In general, the prophylactic dose is smaller than the therapeutic dose.

Definite indications include the following: dirty, traumatic wounds; burns; influenza, during an epidemic when complicating bacterial pneumonia is frequently observed; known exposure to gonorrhea; cases of rheumatic or congenital heart disease for twenty-four hours before and seventy-two hours following dental extraction, tonsillectomy or any operative procedure that might permit the entrance of bacteria into the blood stream (in the hope of preventing bacterial endocarditis); and contamination of the peritoneal or pleural cavities.

Questionable indications include the following: the prevention of scarlet fever or hemolytic streptococcus infection in a person with known exposure, for whom the disease would constitute a serious hazard; under certain conditions, as a prophylactic against the activation of rheumatic fever by preventing hemolytic streptococcus infection of the pharynx (the use of the drug under these circumstances must be decided on the merits of the individual case; such prolonged administration as is necessary for good effects may be harm-

ful per se and certainly is not without risk[4]; more evidence is needed on this score[5]); and inlying catheter, that is, patients on constant bladder drainage (this practice is justifiable for a period of a week or so).

Contraindications

Infections Not Responding to Sulfonamides

Such infections exist, and constitute an important contraindication to the use of these drugs, when a definite diagnosis can be made. When it is known that the therapy will do no good, will only serve to make the patient more uncomfortable, and may complicate his illness, the doctor should have sufficient courage to avoid giving it, even though the family may want to know why the patient is not receiving a sulfonamide drug. Certain diseases in which these drugs have no favorable effect are as follows: "virus" or atypical pneumonia and psittacosis; influenza, in the absence of secondary bacterial infection; common cold; typhoid fever; typhus and Rocky Mountain spotted fever; infections due to neurotropic viruses (poliomyelitis and encephalitis); acute exanthemata in the absence of bacterial infection; infectious mononucleosis, in the absence of secondary infection; puerperal infections due to anaerobic streptococci; urinary-tract infections due to enterococci; toxic manifestations of scarlet fever; diphtheria; and tetanus. In certain other diseases, such as tularemia and brucellosis, the evidence that the sulfonamides do more than produce temporary improvement is scanty, but they probably deserve a trial for several days.

Mild Illness or Localized Infection

One of the truths which was apparent to former physicians who had few specific remedies was that most patients got well if let alone and given a reasonable chance. This simple fact seems to have been forgotten, and there is a growing tendency to replace the therapeutic nihilism of former years with therapeutic overenthusiasm, aided and abetted by the glowing reports of new remedies to be found in popular magazines and the attractive brochures that arrive by the score in each week's mail.

The sulfonamides are not very effective, particularly against organisms like the hemolytic streptococcus, when there is no fever and the inflammatory process is indolent. Thus, attempts to rid the throat of hemolytic streptococci in the absence of symptoms or to treat a mild attack of acute tonsillitis with one of the sulfonamides are usually doomed to failure. The evaluation of treatment in tonsillitis requires great judgment. Although studies have indicated that the sulfonamides have little effect on the disease,[6] some observers feel quite confident that its severe complications can be reduced in frequency and successfully combated by chemotherapy. I rarely use the sulfonamides unless the temperature exceeds 102°F. or there is evidence of extension of the infection, such as sinusitis, adenitis or otitis media. On the other hand, in cases of acute nephritis, sulfanilamide has been recommended as a means of diminishing focal streptococcal infection, particularly in the tonsils.[7] Its main virtue is to reduce the number of bacteria and to make possible the early extirpation of the focus without producing a flare-up. In such cases it should only be used under very close supervision.

Localized infection, associated with the accumulation of pus, is resistant to sulfonamides, because of the inhibitor present in the pus. The drugs are very effective in aiding the localization of spreading infections, but once localization takes place they may have little effect in actually getting rid of bacteria. Thus, in puerperal sepsis, hemolytic streptococci are usually found in the lochia long after sulfonamides have cured the disease. If all the pus can be removed from an abscess, such as an empyema cavity, the sulfonamides may then assist cure without resort to surgery,[8] but the total removal of pus is often technically impossible by aspiration. A three-day course of chemotherapy starting twelve hours before incision of a severe purulent infection such as a carbuncle, may occasionally be worthwhile in an attempt to prevent metastatic infection from the trauma of operation.

Previous Severe Toxic Reactions to Sulfonamides

These drugs are now being used so extensively that a physician should always ask the patient whether he has had them before starting therapy, and if so, how he tolerated them. If he had a severe reaction, the physician should use a different sulfonamide and proceed with some caution. I believe that intensive chemotherapy with a different sulfonamide drug should be used if the patient is desperately ill. If, however, treatment can be deferred for a short time, he should be given a test dose of 0.5 gm. of the drug. If no untoward symptoms appear in twelve hours, full doses can probably be safely used. Even if a patient has had no reaction to a previous course of sulfonamide therapy, particularly a short one, the physician should be on the alert for toxic reactions during a second course. I recall a patient who developed high fever within twelve hours of the start of a course of sulfathiazole for a urinary tract infection. On careful inquiry it was found that she had received sulfathiazole six months previously. This course had produced sensitization, but since it lasted only four days,

all the drug was excreted before she became sensitive, and hence no reaction occurred at that time. Sensitivity persisted, however, and she developed an accelerated reaction when the drug was readministered six months later.

Acute Rheumatic Fever

Patients with this disease actually become sicker when sulfonamides are given.[9, 10] The drugs may also be dangerous in certain cases of acute disseminated lupus erythematosus.[11]*

Leukopenia

At this point, it is worth emphasizing that leukopenia or agranulocytosis is *not* a contraindication to sulfonamide therapy in cases of severe pyogenic infection. In overwhelming pneumococcal, hemolytic streptococcus or staphylococcal infections, the white-cell count may be depressed to levels of less than 1000, with almost complete absence of polymorphonuclear leukocytes. Whenever a physician meets this situation, he should bear in mind the possibility of leukemia. However, this depression of the bone marrow can occur in severe infection. From the standpoint of therapy it is an indication for immediate, intensive chemotherapy, since it is a grave prognostic sign. The circulars on pneumonia therapy issued by the Massachusetts Department of Public Health in years past have stated that leukopenia is an indication for serum therapy and a contraindication to chemotherapy. This, I believe, is entirely wrong. Serum therapy acts only by making possible phagocytosis of pneumococci by leukocytes in the lung and by the reticuloendothelial cells lining the vascular system. The number of circulating polymorphonuclear leukocytes is no indication of their number in the lung lesion, where their action on the pneumococci must take place, but presumably there will be fewer at the spreading margin of the lesion if there are very few in the peripheral blood. Therefore serum therapy is apt to be less effective in such cases. On the other hand, chemotherapy, which attacks the organisms themselves and can destroy pneumococci without the intervention of white blood cells in the pneumonic lung,[12] is the most effective form of treatment, since it stops the multiplication of the organisms, which is responsible for the bone-marrow depression. In such severe cases of pneumonia, combined therapy is probably most effective, so that once intensive chemotherapy is under way, serum should also be used. This of course applies to leukopenia before chemotherapy begins. Leukopenia appearing after chemotherapy has been instituted, when the patient is improving, is usually due to the drug itself.

*Although sulfonamides should not be given for the treatment of rheumatic fever itself, they should not be withheld from rheumatic patients when there is a clear indication, such as septicemia or pneumococcal pneumonia.

II. Which sulfonamide drug should be used?

There are several factors to be weighed in the choice of a sulfonamide drug for the treatment of any particular case. These are the relative efficiency of the different drugs in the particular infection; the previous experience of the patient with sulfonamides; and pharmacological considerations.

The relative efficiency of the different drugs in different types of infection is partially covered by Table 1. In general, sulfanilamide is less potent than the other sulfonamides, except perhaps against Group A hemolytic streptococci, so that it should be used only in infections due to the latter organism or where its high diffusibility and lack of toxicity for the kidney are assets that outweigh its drawbacks. Sulfanilamide is ineffective in pneumonia, and gives comparatively poor results in gonorrhea. There are few bacteriologic reasons for selecting one of the three substituted sulfonamides over the others, except in the case of infections due to staphylococci, Clostridia or gram-negative enteric bacilli, where sulfathiazole seems to have a slight advantage. In general, sulfathiazole and sulfadiazine possess somewhat greater potency than sulfapyridine.

The previous experience of the patient is important, and if he has had toxic reaction to a given drug, the physician should use a different one. This is one of the best reasons for having three different substituted sulfonamide drugs available.

Pharmacological considerations weigh most heavily in the choice of a drug. Neither sulfanilamide nor sulfapyridine should be used routinely, because of the subjective discomfort they produce in the patient, either malaise, headache and anorexia or nausea and vomiting. Sulfathiazole and sulfadiazine are much better tolerated. However, sulfanilamide is recommended in the treatment of acute hemorrhagic nephritis because it rarely injures the kidney. It is useful also for subcutaneous or intrathecal administration, and may be employed to initiate chemotherapy in meningitis because it enters the spinal fluid so readily.

In general, sulfadiazine is the drug of choice in the systemic chemotherapy of all types of infection, with the following possible exceptions:

Urinary tract. Sulfathiazole is potent in small doses against the common organisms causing this type of infection. It is rapidly excreted in the urine in high concentrations and hence gives best results on the smallest dosage.

Gonorrhea. In this disease, sulfathiazole and sulfadiazine give equally good results. It seems worth while, however, to use sulfathiazole and to save sulfadiazine for more serious infections,

when its lack of side effects may be very helpful, because large doses must be given.

Staphylococcal infections. Sulfathiazole is probably the most potent drug (except penicillin,[13] which unfortunately is not yet generally available) against this stubborn and dangerous organism.

Gas gangrene. Sulfathiazole has a wider range of effectiveness against Clostridia, particularly *Cl. septique*, than the other sulfonamides.

Anthrax. Sulfathiazole and sulfapyridine are reported as better than the other sulfonamides.[14]

In the treatment of meningitis, much has been made of the fact that one drug traverses the blood-brain barrier more readily than another. Sulfathiazole is always present in the spinal fluid in much lower relative concentration than any of the other drugs, whereas the concentration of sulfadiazine in the thecal space rises slowly. For this reason sulfapyridine has been recommended for the treatment of pneumococcal meningitis, and sulfanilamide for hemolytic streptococcus meningitis, since both drugs enter the spinal fluid rapidly. However, success in the treatment of meningitis with sulfathiazole suggests that the concentration of drug in the spinal fluid may not be important except in so far as it reflects its concentration in the tissue spaces. Because treatment in meningitis must frequently be continued for more than ten days, sulfadiazine is probably best, except in staphylococcal infections.

When parenteral administration is used, pharmacological considerations are all-important. For intravenous use, sodium sulfadiazine has great advantages over the sodium salts of sulfathiazole or sulfapyridine. It is excreted much more slowly, so that a patient may be treated by an initial large dose followed by injections of 2 gm. every eight to twelve hours with the maintenance of an effective blood concentration. The rapid excretion of sodium sulfathiazole makes it almost impossible to maintain a satisfactory blood level without producing renal damage, and the same is true to a lesser degree of sodium sulfapyridine. Although both these drugs may be given safely once, repeated doses are dangerous. For subcutaneous administration either 0.5 per cent solutions of the sodium salts of sulfadiazine,* sulfathiazole or sulfapyridine in physiologic saline solution, or else 0.8 per cent sulfanilamide in saline, may be used. The latter is preferable where it is efficacious, since it is rapidly absorbed. When dilute solutions of the sodium salts of the other sulfonamides are given subcutaneously, absorption may be slow and lead to a piling up in the blood after repeated doses. For intrathecal use, *only* 0.8 per cent sulfanilamide should be used, because solutions of the sodium salts are too alkaline; it is doubtful, however, whether intrathecal injection is ever necessary.

*Sodium sulfadiazine may be used in concentrations as high as 2 per cent subcutaneously.

III. What is the dose, and how shall it be given?

As has been previously stated, the blood concentration depends on the balance between the rate at which the drug is entering the circulation, usually from the bowel, and the rate at which it is being cleared in the urine. A large initial dose is given, so that the blood level rises rapidly to an effective concentration, and from then on doses are given so as to maintain that concentration by balancing the amount excreted by the kidney. The rate of clearance by the kidney depends on the functional capacity of that organ. The physician should always try to assess renal function by questioning the patient about nocturia and previous nephritis and by examining the urine.

In the presence of normal renal function, the excretion of sulfanilamide is hastened by an increase in the urinary output. With the other sulfonamides, the rate of excretion of the drug is influenced to a much lesser extent by the urinary output. Therefore, when giving sulfanilamide the fluid intake is usually restricted to 2500–3000 cc., whereas with the other drugs fluids are forced, to prevent concentration of the urine and precipitation of the free or conjugated drug in the kidney.

One of the commonest errors is too small dosage. A little sulfonamide treatment is worse than none, because it either has no effect or partially suppresses the infection, whereas the organism has a chance to develop some degree of sulfonamide resistance. It prolongs the period of chemotherapy and thus increases the chances of serious toxic reactions. Once the decision to use chemotherapy is made, the physician should try to get the infection under control as rapidly as possible.

The route of administration should always be oral if possible. This assures slow, steady absorption, and hence a more constant blood level. In patients who are unable to swallow the tablets, they should be pulverized and suspended in a little water, milk or fruit juice. In comatose patients — those with meningitis, for example — a nasal tube can be introduced into the stomach and a suspension of the drug in water given through it.

Parenteral administration is indicated under the following conditions:

For the initial dose in patients with very severe infections. Frequently patients who are very ill are distended, and often nauseated. By giving the initial dose intravenously, an adequate blood level is immediately established, and several hours

are saved, which may be vitally important in bringing the infection under control.* Oral administration of the subsequent doses, if possible, assures continuous absorption and maintenance of an effective level.

In patients who are unable to take oral therapy because of vomiting or for surgical reasons. Absorption of these drugs is best in the stomach, so that their administration through a Miller–Abbott tube into the duodenum or jejunum may not be a very reliable method unless carefully controlled by determinations of the blood level. Hence, in severe peritonitis, it is probably best to use parenteral administration.

In patients in whom it is difficult to establish blood levels. In such patients, intravenous doses may be used to supplement oral therapy (Case 2).

It must be emphasized that prolonged intravenous injection of the sodium salts of the substituted sulfonamide drugs carries a high risk of renal complications because of the massive excretion of the drug resulting from the high blood levels following injection, and close attention must be paid to the fluid intake and urinary output.

Table 2 gives the recommendations for dosage in convenient form for reference. The doses given are for an average 150-pound adult. The dosage for children and larger or smaller patients should be adjusted according to weight. In small children, somewhat larger doses in proportion to body weight are used.

In patients with diminished renal function, the clearance of sulfonamides roughly parallels urea clearance. To establish an adequate level, the initial dose is only reduced to about 80 per cent of the usual one, but subsequent maintenance doses are reduced in proportion to the reduction in renal function, because of the delay in excretion. In such patients, whenever possible, the blood level should be determined frequently, and where facilities are not available, dosage should be reduced as soon as there is a satisfactory therapeutic response.

Very little has been said above concerning the use of the two sulfonamides that have been recommended for strictly intraintestinal chemotherapy, namely, sulfaguanidine[15] and succinyl sulfathiazole or sulfasuxidine.[16] The former is not absorbed to any great extent, but is quite soluble.

TABLE 2. *Dosage Schedules for Average 150-Pound Adult.*

DRUG*	INITIAL DOSE	MAINTENANCE DOSAGE	DESIRED BLOOD LEVEL	FLUID INTAKE	DESIRED URINARY OUTPUT	DOSAGE OF SODIUM BICARBONATE
	gm.†	*gm.*	*mg./100 cc.*		*cc./24 hr.*	
ORAL ADMINISTRATION						
REGULAR DOSAGE FOR GENERAL INFECTIONS						
S.A.	4.0	1–1.5 every 4 hr.	8–15	Restrict	1500	Equal amounts
S.P.	4.0	1 every 4 hr.	5–10	Force	2000	None
S.T.	5.0	1–1.5 every 4 hr.	3–5	Force	2000	None
S.D.	5.0	1.5 every 6 hr.	8–15	Force	2000	None
GONORRHEA, UNLESS SEPTIC COMPLICATIONS EXIST						
S.T.	3.0 (first 24 hr.)	0.5 4 i.d.	—	—	1500	None
S.D.	3.0 (first 24 hr.)	0.5 4 i.d.	—	—	1500	None
URINARY-TRACT INFECTIONS, UNLESS VERY SEVERE						
S.T.	—	0.5 4 i.d.	—	Force	2000	May be used to keep urine alkaline (both drugs more effective in alkaline urine)
S.D.	—	1.0 4 i.d.	—	Force	2000	
INTESTINAL INFECTIONS AND PREOPERATIVE REDUCTION OF BACTERIAL FLORA OF COLON						
Sulfaguanidine	6.0‡	3.0 every 4 hr.	<2			
Sulfasuxidine	5.0‡	2.5 every 4 hr.	<2			
INTRAVENOUS ADMINISTRATION						
S.A.	Not used					
Sod. S.P.	4.0	Shift to oral				
Sod. S.T.	4.0	Shift to oral				
Sod. S.D.	5.0	2.0 every 8–12 hr.	8–15	Force	2000	None
SUBCUTANEOUS ADMINISTRATION						
S.A. (0.8%)	4.0	3.0 every 8 hr.	8–15	Moderate	1500	
Sod. S.D. (0.5–2%)	5.0	2.0 every 8 hr.	8–15	Force	2000	

*S.A. = sulfanilamide; S.D. = sulfadiazine; S.T. = sulfathiazole; S.P. = sulfapyridine.

†For conversion to grains, 1 gm. = 15 gr.

‡Initial large dose probably only necessary in dysentery when diarrhea is present; in absence of diarrhea, dose of 0.25–0.3 gm. per kilogram of body weight may be given daily in three or four divided doses (every 6 or 8 hr.).

*This is very important (Case 6). Enough individuals absorb these drugs irregularly when given by mouth (Case 2) to make it risky to depend on the oral route when starting therapy in a very sick patient.

The latter is probably hydrolyzed in the bowel to sulfathiazole, which is the most potent of the sulfonamide drugs against the coliform organisms and the Clostridia, which make up a large portion of the bacterial flora of the colon. In the lower intestine sulfathiazole is very little absorbed, hence it is largely excluded from the blood. Toxic reactions are apparently more frequent with sulfaguanidine than with sulfasuxidine, perhaps because the former is more readily absorbed. Both drugs are effective in the treatment of bacillary dysentery and of dysentery carriers, and are also effective, when given for about five days preoperatively, in effecting a marked reduction in the bacterial flora of the stools, thereby reducing the likelihood of infection in surgery of the large bowel. In ulcerative colitis, sulfaguanidine has failed to produce much effect, and sulfasuxidine is still on trial. Dosage of either drug should be large, in an effort to saturate the bowel with the drug in solution, which will then be effective wherever it comes in contact with the mucosa. With diarrhea, more frequent and larger doses must be used. If a loop is excluded as with colostomy, the drug must be introduced into the distal loop in order to affect its contents. Prolonged use of either drug should be avoided, since certain essential growth factors, such as biotin, are synthesized to a considerable extent by the bacteria of the bowel.[17]

IV. When should the blood level be determined?

The determination of sulfonamide concentrations in the blood and other body fluids has been of enormous value in putting sulfonamide therapy on a rational basis. However, enough is now known of the pharmacology of these drugs to make the determination of blood concentrations superfluous in many cases. When the patient responds promptly to treatment and has no abnormality of renal function, there is no need for determining the blood level. On the other hand, there are some situations in which it should be determined. These are as follows: when a patient does not respond to therapy in twenty-four to thirty-six hours; when a patient has an abnormality of the urinary tract — diminished renal function or incontinence — so that the output cannot be measured; and when parenteral therapy or administration through a stomach or duodenal tube must be used.

V. How long should therapy be continued?

This question is difficult to answer in general terms. It depends on two factors: the rate of elimination of the drug (dependent on the properties of the drug and the renal function) and the properties of the infecting organism. In general, therapy should be continued until all evidence of infection has disappeared for at least forty-eight hours; in the case of pyogenic infections, until localization has occurred and adequate drainage has been established; or, in certain cases, until sufficient antibody has been developed or administered to the patient to maintain a cure.

Bacterial infections differ in the manner in which recovery takes place. In pneumococcal pneumonia, spontaneous cure is effected by crisis or by lysis, owing to the development of both local and humoral immunity as the result of infection. Administration of serum, in sufficient doses will produce an artificial crisis as soon as sufficient antibody is present.[18] The effective sulfonamides likewise produce either a critical or a gradual fall in temperature. This is because pneumococci are readily destroyed, either by phagocytosis if sufficient antibody is present[19] or by autolysis if their growth is inhibited by the sulfonamides.[12] Therefore, once the temperature has become normal, usually forty-eight hours will suffice completely to eradicate the infection, and the drug may be discontinued at the end of this period. On the other hand, hemolytic streptococci are much harder to destroy, and therapy must be continued longer after the temperature has become normal if relapse is to be prevented. In the case of erysipelas or cellulitis, evidences of local infection, such as local redness and edema, may persist after the temperature becomes normal, and chemotherapy should be continued until these disappear. In cases of deep infection, such as mastoiditis and osteomyelitis, it may be impossible to detect evidence of continued infection by any method, and the decision of when to stop the administration of the sulfonamides is very difficult. Such aids as x-ray examination and determination of the sedimentation rate must be used, and therapy should be continued for about two weeks after apparent cure.

Staphylococcal infections are notoriously resistant to all forms of therapy. In such cases, chemotherapy can only be an adjunct, which aids in the localization of the infection and in the clearing of the blood of organisms, and which helps to prevent the development of new foci, particularly in the kidney. Sulfathiazole should be used until adequate localization occurs, the blood is sterile and the focus is draining either spontaneously or as the result of surgical intervention. In meningitis, temperature is a notoriously poor index of recovery, and many patients who do recover will run a fever for a week or two after recovery really occurs. The spinal-fluid findings are most reliable. When all polymorphonuclear leukocytes disappear from the spinal fluid, it is probable that the infection

has been overcome, and the dosage may be reduced over a period of several days. If no signs of recurrence appear, the drug is then discontinued (Case 4).

Chronic infections, such as actinomycosis or subacute bacterial endocarditis, necessitate the continuation of chemotherapy for weeks or months, even though a patient may seem well. In acute infections the aim should be to cure the disease in less than ten days if possible, as serious toxic reactions are much less frequent during this period.

VI. What should be done if there is no response to therapy?

If fever continues despite thirty-six hours of adequate chemotherapy, certain possibilities should be immediately checked.

Incorrect diagnosis. This is perhaps the most frequent reason for therapeutic failure. For example, what is taken to be pneumococcal pneumonia may actually be so-called "atypical" or "virus" pneumonia, pulmonary infarction or typhus fever, none of which respond to chemotherapy. Therefore, the diagnosis should always be checked in such cases, particularly with reference to the bacteriology of the case.

Inadequate blood level. The blood level should be determined, or if this is impossible, and there is no other reason for the failure of therapy, the maintenance dose should either be increased or a single supplementary dose of 2 or 3 gm. of sodium sulfadiazine given intravenously to raise the level promptly (Case 2).*

Presence of pus. This should always be suspected when a patient fails to respond to therapy and continues to run fever. The following case illustrates this very clearly.

CASE 2 (P.B.B.H. M61660 and S69469). The patient, an 18-year-old boy, who had had chronic sinusitis for 5 years, was admitted on the 3rd day of an illness characterized by coryza, cough with blood-streaked sputum and pleuritic pain over the right side of the chest. On admission the temperature was 101.2°F., the pulse 110, the respirations 52, and the white-cell count 19,800. Examination of the chest showed signs of fluid or consolidation on the right, and x-ray films revealed patchy consolidation of the right lower lobe with haziness at the base, interpreted as representing bronchopneumonia with pleurisy. A blood culture was sterile, and a Type 19 pneumococcus was isolated from the sputum.

Despite large doses of sulfadiazine, 5 gm. initially and 1.5 gm. every 4 hours (later increased to 2 gm.), the temperature fluctuated between 101.2 and 103.6°F., the white-cell count rose to 39,000, and signs of fluid, both by physical examination and x-ray study, became increasingly prominent. The chest was tapped on the 4th and 8th days, and after a long delay, growth of Type 19 pneumococcus was obtained. Therefore, the patient was submitted to closed intercostal drainage on the 8th day, rib resection on the 12th day, and again on the 28th day, before the temperature finally subsided and recovery took place. Sulfadiazine was discontinued after the second operation.

Comment. This case illustrates three points particularly: first, the difficulty experienced in achieving satisfactory blood levels on oral therapy alone in occasional cases; second, the necessity for checking blood levels and looking for pus when there is no therapeutic response; and third, the failure of sulfonamide therapy when there is an accumulation of pus. Despite large doses of sulfadiazine by mouth (5 gm. initially and 1.5 gm. every 4 hours), the blood level was only 3.0 mg. per 100 cc. after 24 hours of therapy. Therefore, the dose was increased to 2 gm. every 4 hours, with a rise in the level to 7.0 mg. per 100 cc. Since this was considered too low, and the infection was not yielding to treatment, an additional 2 gm. of sodium sulfadiazine was given by vein. The next day the level was 11 mg. per 100 cc., but fever continued, and on the following day pus was found in the chest.

Drug fever. Frequently the cause of continued fever in a patient receiving sulfonamide therapy is the drug itself. Of all the problems raised by the introduction of these remedies into clinical medicine, the confusion caused by drug fever is most constantly cropping up. There is no way to be certain when fever is due to the drug. However, if it occurs after the patient has apparently been cured, is accompanied by rash, adenopathy and arthralgia, and is characterized by a paucity of symptoms, relative bradycardia and a normal white-cell count, the diagnosis is simple. Unfortunately, both tachycardia and leukocytosis may occur (Case 6).

Drug fever may be associated with chills, which usually come on soon after the tablets are swallowed, delirium, extreme headache and malaise, or may be practically asymptomatic. The fever may be low grade, septic in type, or high and sustained. It usually begins from the fifth to the twelfth day after treatment is started, and is most confusing when it complicates a disease that responds slowly to therapy, such as staphylococcal infection, so that drug fever is superimposed on the fever due to the infection itself. As already mentioned, if a patient has previously had a course of sulfonamide therapy, and has become sensitized, he may develop drug fever within a few hours after receiving the drug a second time.

The best way to present the problem of drug fever is to cite a number of cases that have occurred in my own experience.

CASE 3 (P.B.B.H. S63445) (Fig. 2). This 26-year-old man was admitted for treatment of an acute urethritis and prostatitis of 5 days' duration. Gram-negative intracellular diplococci were present on smear, and the gonococcus was

*In certain patients an unusually large percentage of the circulating sulfonamide is present in the acetylated form. This is not therapeutically active, nor is it measured by the ordinary blood-level determination. In cases of inadequate level, when good-sized doses have been given, it is worth while, if possible, to determine both the free and the total sulfonamide to check on this possibility.

isolated from the prostatic secretion. He was placed on very large doses of sulfanilamide and did very well, with disappearance of the urethral discharge and of gonococci by culture. However, the blood level rose to 16 mg. per 100 cc. of sulfanilamide as a result of the large doses,

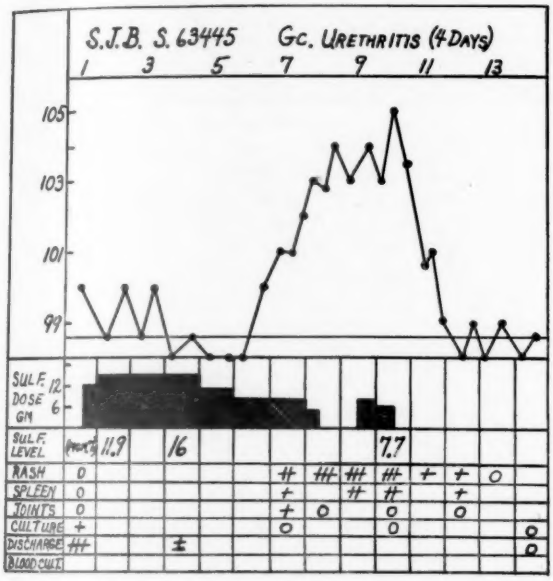

FIGURE 2. *Clinical Course of Case 3.*

and on the 6th and 7th hospital days the temperature rose, reaching 104°F. on the 8th day. With this fever, the patient developed transient pains in the metatarsal region of the right foot, a purplish, blotchy rash and a palpable spleen. The drug was stopped temporarily, but, because the temperature did not fall, its administration was resumed on the 9th and 10th days. With this the patient had a shaking chill, the temperature rose to 105°F., the rash became more prominent, and the spleen remained palpable. The first diagnosis had been drug fever, but because of failure of the fever to remit on stopping the drug, the physician felt that the patient probably was developing gonococcal septicemia. When the drug was stopped for a second time and large amounts of fluid were given by mouth and by vein, the temperature soon fell to normal and the rash disappeared.

Comment. This is a classic example of severe drug fever, with onset on the 6th day, rash, arthralgia and splenomegaly. The high, flat temperature is quite characteristic of the severe form of intoxication. The chill on readministration of the drug is likewise frequently observed. Nevertheless, the physician in charge of the patient feared that the patient was suffering from an extension of his infection to the blood stream. Since this had occurred in the face of a high blood-sulfanilamide level, there would have been no sense in continuing the drug even if the symptoms had thus been correctly interpreted.

CASE 4 (P.B.B.H. M61218). This 17-year-old boy was admitted because of drowsiness, headache and vomiting for 24 hours. He was found to have classic signs of meningitis, with a white-cell count of 33,200. A lumbar puncture showed markedly increased pressure and cloudy, yellowish fluid containing 12,500 cells per cubic millimeter, nearly all polymorphonuclears. Culture of the spinal fluid yielded Type 1 meningococci. In the first 24 hours the patient was given 10 gm. of sodium sulfadiazine intravenously because of incessant vomiting, which prevented oral therapy. Thereafter he received 1 gm. of sulfadiazine by mouth every 4 hours for 3 days. On this regime the pulse fell from 120 on admission to an average of 60, the temperature from a range of 100–102°F. on the 1st day to 99–100°F. on the 4th day. Since the blood level was only ranging from 2.7 to 6.6 mg. per 100 cc. with a spinal fluid level of 2.4 mg. per 100 cc., and the patient was complaining of a return of headache, the dose was increased to 1.5 gm. every 4 hours. Thereafter the level ranged from 10–13 mg. per 100 cc., and he made steady improvement. On the 8th day, the dose was reduced to 1 gm. every 4 hours, and on the 10th day to 1 gm. every 6 hours. The white-cell count remained normal after the first 2 days, and lumbar punctures revealed a steady decrease in the number of cells. On the 3rd day only about 300 per cubic millimeter were present, of which 30 per cent were lymphocytes, and cultures were negative. On the 8th day there were 37 cells, all but one of which were lymphocytes, and consequently the dose of sulfadiazine was reduced. From the 9th day on, the patient began to run an afternoon fever of 99.5°F. for 3 days, then rising to 100°F., and from the fifteenth to the seventeenth day reaching 101°F. The spinal fluid still showed only a few lymphocytes, but the initial pressure was high (300 mm. of water), and the dynamic reactions were rather sluggish. Although it was feared that the patient might be developing a localized focus of infection in the meninges or a partial block because of the increasing fever and lack of symptoms, the drug was discontinued. Within 36 hours the temperature became normal, but the white-cell count fell to 4000 and a typical maculopapular rash of the erythema nodosum type developed over the extremities, which disappeared in 4 days.

Comment. This type of low-grade septic fever is most confusing. All forms of purulent meningitis are notoriously prone to relapse after sulfonamide therapy; hence the administration of the drug was continued for a long time after all other evidence of infection except fever had disappeared. The prompt subsidence of fever when the drug was discontinued, coupled with the appearance of rash and leukopenia, makes it very likely that the drug was the cause.

CASE 5 (P.B.B.H. M58886) (Fig. 3) (previously reported by Michael[20]). This 35-year-old woman developed chills, headache and general malaise with a fever of 101°F. 6 days before entry. These symptoms with prostration persisted until 2 days before entry, when she began to feel worse. She developed cough, with the production of large amounts of dark-brown sputum, and noticed soreness in her right side. On admission, the temperature was 104°F., the white-cell count 10,900, and examination revealed signs of consolidation at the right base. Subsequent bacteriologic studies revealed virulent *Staph. aureus* in pure culture in the sputum, and a diagnosis of staphylococcal pneumonia complicating influenza was made. Serologic evidence for recent infection with influenza A virus was obtained from her blood. This type of infection was known to be severe and resistant to therapy, so large doses of sulfathiazole (1.5 gm. every 4 hours) were given and a blood level ranging from 6.4 to 9.8 mg. per 100 cc. was achieved.

Although the temperature tended downward the first 3 days, thereafter it rose gradually, reaching 105.4°F. on the 12th day, with a pulse of 120 and a white-cell count of 7100 (24,000 on the 8th day). With this increase in

temperature, the patient appeared sicker, with signs of consolidation involving more of the right lung and the left base as well (confirmed by x-ray study), and continued to cough with production of large amounts of tan-colored, blood-streaked sputum. However, on the 13th day she appeared slightly better, although the temperature was

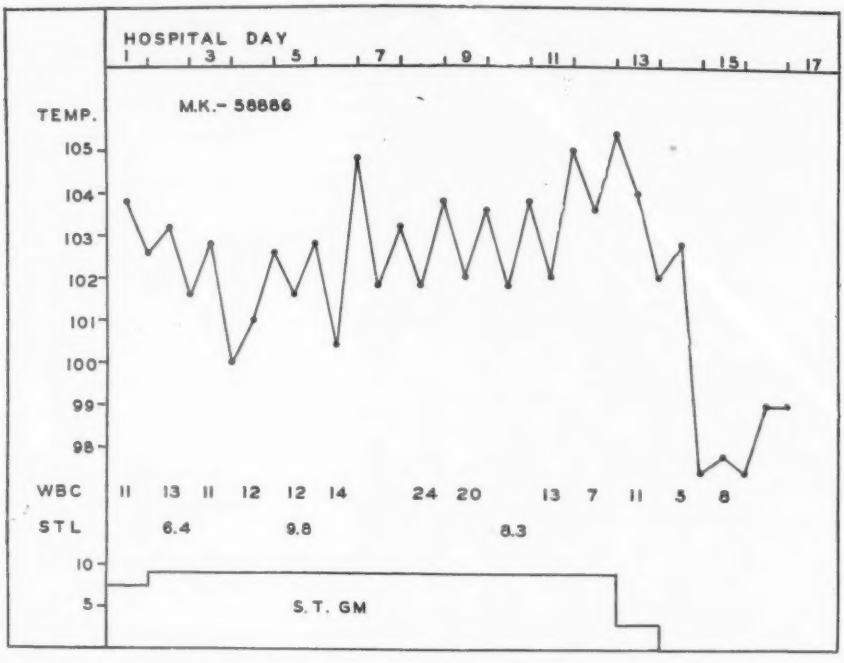

FIGURE 3. *Clinical Course of Case 5 (reproduced by permission of the* Journal of the American Medical Association*).*

104°F., and in view of the high, sustained fever, the fall in the white-cell count, and the slight improvement of chest signs, it was decided to discontinue sulfathiazole. The next day the temperature fell precipitously to normal, the white-cell count went down to 4600, and the patient began an uneventful convalescence.

Comment. There seems little doubt that severe drug fever was superimposed on a very severe infection. Where one began and the other ended is impossible to determine. It is not at all impossible that fever, due to the drug, with its potentiation of the bacteriostatic action of the sulfonamides, actually aided this patient in recovering from this severe disease. This case illustrates the rapid recovery from toxic reactions to sulfathiazole when the drug is stopped.

CASE 6. The patient, a 30-year-old white woman, had an uneventful term delivery of her second child. Two days post partum she developed abdominal cramps, anorexia and a fever, which rose rapidly to 105.8°F. with a pulse of 160. The white-cell count was 18,000. She was given 1 gm. of sulfadiazine followed by 2 gm. in 4 hours, and 1 gm. every 4 hours thereafter for the next 24 hours, without any effect on her condition. When seen in consultation, the temperature was 104.8°F., the pulse 160, and the blood pressure 60/40. The patient was acutely ill, breathing with difficulty. There was a diffuse scarlatina-form eruption, and petechiae appeared at any points of trauma. The pulse was thready and rapid, and the abdomen, which was distended, showed marked tenderness in the lower quadrants. A presumptive diagnosis of puerperal sepsis due to scarlatinal hemolytic streptococci was made, and 4 gm. of sodium sulfathiazole and 18,000 units of scarlatinal antitoxin were given by vein. In the next 6 hours two more doses of 2 gm. of sodium sulfathiazole were given intravenously, as well as large amounts of 5 per cent glucose in saline, since the patient had not voided for 12 hours. Within 12 hours after starting intravenous sodium sulfathiazole, the temperature was 99°F. Because of the circulatory collapse, 500 cc. of reconstituted dried plasma was given after the temperature began to fall and the blood pressure rose first to 95/55, when the patient began to void again, and then to 125/80.

A subsequent blood culture, taken before sodium sulfathiazole was given, showed gram-positive diplococci that looked like staphylococci, but were not finally identified. The blood level after the 8 gm. of sodium sulfathiazole was 32 mg. per 100 cc. For the next 17 days sulfathiazole was continued by mouth and the patient made slow progress, despite the development of an acute nephritis, probably due to a combination of sulfathiazole and her infection, and of a spontaneous pneumothorax, which required aspiration of air on repeated occasions. Because she developed some delirium on the 17th day, and there seemed to be no more abdominal tenderness, sulfathiazole was discontinued.

For the next 12 days the patient did very well. However, she then developed pain over the bladder, coming on after voiding. The physician, fearing that she was getting a bladder infection, gave her 1 gm. of sulfathiazole, which was repeated every 4 hours. Despite this, the temperature rose steadily to 104°F., with rapid pulse and respiration. At this time physical examination was negative except for a diffuse bright-red erythema. The white-cell count was 19,000, with 91 per cent polymorphonuclear cells. Questioning revealed that 1 hour after the first dose of sulfathiazole the patient developed epigastric distress and vomited. A diagnosis of drug fever was made, the sulfathiazole was discontinued, and fluids were forced. In 18 hours the temperature had fallen to 102°F. and the

white-cell count to 10,000. Shortly thereafter the temperature rose to 104°F., but the patient felt better. In 36 hours after stopping the drug the temperature became normal and the patient felt entirely well again. From then on, recovery was uneventful.

Comment. This case illustrates many points about chemotherapy. First, the patient was given entirely inadequate doses of sulfadiazine when she was obviously suffering from a fulminating case of puerperal sepsis. Therefore, heroic measures were necessary and she was given massive doses of intravenous sodium sulfathiazole. That these were massive was shown by the blood level of 32 mg. per 100 cc. after 8 gm., due no doubt to the anuria, which resulted from the circulatory collapse with low blood pressure. As a result of this heroic therapy, the temperature fell to normal in 12 hours. The response of the shock state to plasma, which restored both blood pressure and urinary output, was due to the fact that the infection had already been brought under control. The nephritis that followed, characterized by fixed specific gravity, heavy albuminuria and hematuria, with many granular casts consisting of masses of sulfathiazole crystals, was typical of the direct renal injury produced by the drug. The final episode of fever on a second administration of sulfathiazole was a typical accelerated reaction due to previous sensitization. The rash, leukocytosis and high fever were sufficiently like the onset of the infection, however, to make the decision difficult.

Case 7 (P.B.B.H. M61859) (Fig. 4). This 44-year-old Italian bartender, who had been a heavy drinker for years, caught cold and lost "pep" and 20 pounds in weight in

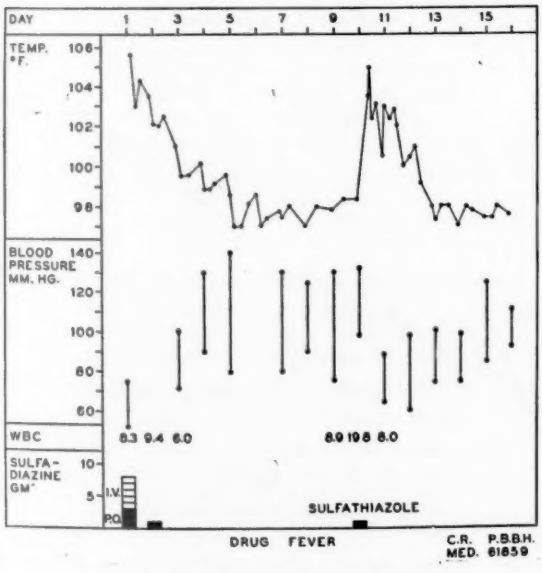

Figure 4. *Clinical Course of Case 7.*

the month before admission. Six days before entry he became much worse, with the development of headache, chills, pain in the left side and increased cough with dark blood-streaked sputum. Three days before entry he had to take to his bed, because he felt dizzy and exhausted. On admission the temperature was 105.6°F., the pulse 120, the respirations 30, the blood pressure 75/50, and the white-cell count 8300, with a shift to the left. There were a generalized reddish flush to the skin, musical rales in both lungs, a little dullness at the right base, abdominal distention and a rapid, weak pulse. On admission a diagnosis of lobar pneumonia was made, and because the patient was so ill, intravenous sodium sulfadiazine followed by oral sulfadiazine was given, and the blood level rose to 14.5 mg. per 100 cc. However, since the sputum failed to show pneumonococci, a blood culture was negative, and the chest was clear on x-ray examination, the drug was discontinued, and the temperature fell to normal in 3 days with a concomitant rise in blood pressure. An electrocardiogram the day after admission showed intraventricular block, but 5 days later, after intramuscular thiamine therapy, the curves were normal. Therefore, in view of the patient's occupation and his story of loss of strength, a diagnosis of acute beriberi with cardiac manifestations was made in retrospect.

At this point careful questioning of the patient and his physician revealed that he had acquired gonorrhea 2 weeks before entry, for which he had been treated with sulfathiazole in full dosage. Shortly before entry he developed fever, and therefore his physician told him to discontinue the drug, but since he became worse he entered the hospital. This made it seem most likely that the patient had severe drug fever on admission. Fortunately, he had been given sulfadiazine, and not sulfathiazole, on entry, or he might have died.

Since it seemed important to know whether the patient was extremely sensitive to the sulfonamides, it was decided to test him with a small dose of each of the drugs. On the 10th hospital day he was given 1 gm. (2 tablets) of sulfathiazole. Within an hour the temperature and pulse began to rise, and in 3 hours he had a severe shaking chill lasting 45 minutes. Eight hours later the temperature was 105°F., the pulse 120, and the blood pressure 104/80, and he was acutely uncomfortable, complaining bitterly of headache. The skin was a fiery red and the conjunctivas markedly reddened. High fever continued for 36 hours, with persistence of the rash and a state of circulatory collapse, with the blood pressure about 90/65 most of the time, despite abundant intravenous fluids, 500 cc. of plasma, adrenalin and aspirin. An electrocardiogram taken on the 2nd day of the reaction showed paroxysmal right bundle-branch block. On the 4th day after the test dose of sulfathiazole the temperature returned to normal, and on the 6th day the blood pressure returned to its usual level (125/85). The white-cell count rose to 19,800 at the height of the reaction and the next day was 8000, with 92 per cent polymorphonuclear leukocytes. Albumin, red cells and casts were noted in the urine during the reaction. Needless to say, tests were not made with the other sulfonamide drugs.

Comment. This case illustrates both how confusing drug reactions may be to the physician who first sees a patient during the reaction, and also how serious they may be, at least with sulfathiazole. This case seems to show that sulfadiazine may be tolerated by patients exquisitely sensitive to sulfathiazole, since this patient improved rapidly when given sulfadiazine intravenously and orally.

Certainly the best diagnostic criteria for drug fever are the absence of other adequate causes for fever and its appearance five to fourteen days after the start of therapy.

VII. What precautions should be observed in the care of patients receiving sulfonamide therapy?

With the substituted sulfonamides now in common use, only three serious toxic reactions occur with much frequency—fever, leukopenia and oliguria. The temperature should be taken at least twice daily to guard against fever. Leukopenia rarely occurs before the tenth day of treatment, therefore, every effort should be made to end treatment by this time, particularly if the patient is ambulatory. After ten days a close check must be kept on the white-cell count, with determinations every two days. Oliguria is most apt to occur in the period of intensive therapy. The appearance of red cells or granular casts in the urine should serve as a warning that this toxic reaction is imminent, but the best precaution is to observe the urine output in twelve-hour periods. When this falls below 800 cc., fluids should be forced intensively. Sulfathiazole, particularly, may cause complete anuria without the appearance of hematuria. Crystals of the drug mean nothing in a routine urine examination, since these drugs crystallize at room temperatures, but the presence of large numbers of crystals in a freshly voided specimen means that the patient needs either more fluids or a smaller dose.

One point that cannot be emphasized too strongly is that leukopenia or drug fever may occur after the administration of a sulfonamide has been stopped. This is particularly true of sulfadiazine, which is the most slowly excreted, and is to be feared in patients with poor renal function, who rid themselves of any of these drugs very slowly. Sulfathiazole, although it produces toxic reactions more often than does sulfadiazine, is excreted very rapidly, so that if a reaction occurs (except oliguria) it is possible to get rid of the offending drug very quickly. This usually produces prompt recovery from the toxic effect (Case 5). On the other hand, with sulfadiazine several days are needed for its elimination. Case 8 illustrates this serious drawback to its use. Because of the possibility of delayed reactions after the cessation of therapy, the white-cell count and the patient's condition should be checked three and five days after treatment is discontinued. Failure to observe this rule will sooner or later lead to trouble.

Case 8 (P.B.B.H. M62187) (Fig. 5). This 56-year-old woman with a history of chronic sinusitis developed fever and rapid respirations within a few hours of an operation on the 3rd hospital day. By the next morning the temperature was 103°F., the pulse 110, the respirations 40, and the white-cell count 19,000. A practically pure culture of *Staph. aureus* was obtained from the throat (she could raise no sputum). The patient was cyanotic and there were signs of consolidation in the right lower lobe. A diagnosis of postoperative pneumonia due to *Staph. aureus* was made, and sulfadiazine was given in large doses, starting on the 5th hospital day. Her temperature fell slowly but steadily, in an entirely satisfactory manner for a patient with a staphylococcal infection. On the 17th day the white-cell count was 9000, the chest signs had cleared, and the patient seemed fairly well. Because the temperature still showed some elevation, the dose of sulfadiazine was reduced, as it was difficult to tell whether this fever was due to the drug or to infection. Since the temperature decreased after this, the drug was discontinued on the 21st day. At this time the white-cell count was 5000 and the temperature normal. Two days later the count was still 5000, the temperature still normal, and the patient was sitting up.

On the 26th day the patient complained of slight sore throat and malaise, developed chills, and by the next day her temperature was over 105°F. and she looked very ill. The white-cell count showed 1250 cells, and on smear no polymorphonuclear leukocytes were seen. This was 6 days after chemotherapy had been discontinued. Despite Pentnucleotide, liver extract, transfusion and vitamins B and C, the patient became steadily worse, the white-cell count failed to rise significantly, fever continued, and she died on the 29th day. Autopsy confirmed the clinical impression that the pneumonia had been cured, and revealed hyperplasia of the bone marrow and an acute enteritis. Post-mortem and two ante-mortem blood cultures were sterile. On the day of death the blood sulfadiazine was 0.79 mg. per 100 cc.

Comment. This case proves in a tragic way that serious toxic reactions may occur a considerable time after the period of chemotherapy. The drug was stopped at a time when there was no reason to suspect that anything was wrong. The white-cell count of 5000, although low, was no lower than is frequently seen when a patient is recovering on sulfonamide therapy and was no lower 2 days later. Perhaps the only sign of impending trouble was the slight unexplained fever after the 15th day; but from the 22nd to the 26th day the patient seemed entirely well. The slow excretion of sulfadiazine and its possible dangers are dramatically illustrated by this case.

The following outline presents a recommended routine in using the sulfonamides:

A. *Before administration*:
   1. Inquire about previous sulfonamide therapy and toxic effects.
   2. Assess renal function (possible nocturia, frequency, history of nephritis; urinalysis).
   3. Determine hemoglobin level and white-cell count.

B. *Administration to ambulatory patients (small doses)*:
   1. Instruct the patient about
      a. Name of drug.
      b. Importance of regular doses.
      c. Importance of adequate fluids and check on volume of urine output.
      d. Possibility of toxic reaction (report untoward episodes).
      e. Dangers from slow reaction time in crossing streets, driving car and so forth.

2. Arrange check-up visits at 3, 7 and 10 days; after 10 days the patient should be seen three times a week up to 6 weeks, then weekly so long as the drug is continued.

Check-up should include examination of the mucous membranes for pallor, scleras for icterus and skin for rash, a temperature reading and inquiry about malaise, nausea and urinary output. If the last is low, urinalysis should be done. A white-cell count should be made, and if below 6000 a blood smear should be examined.

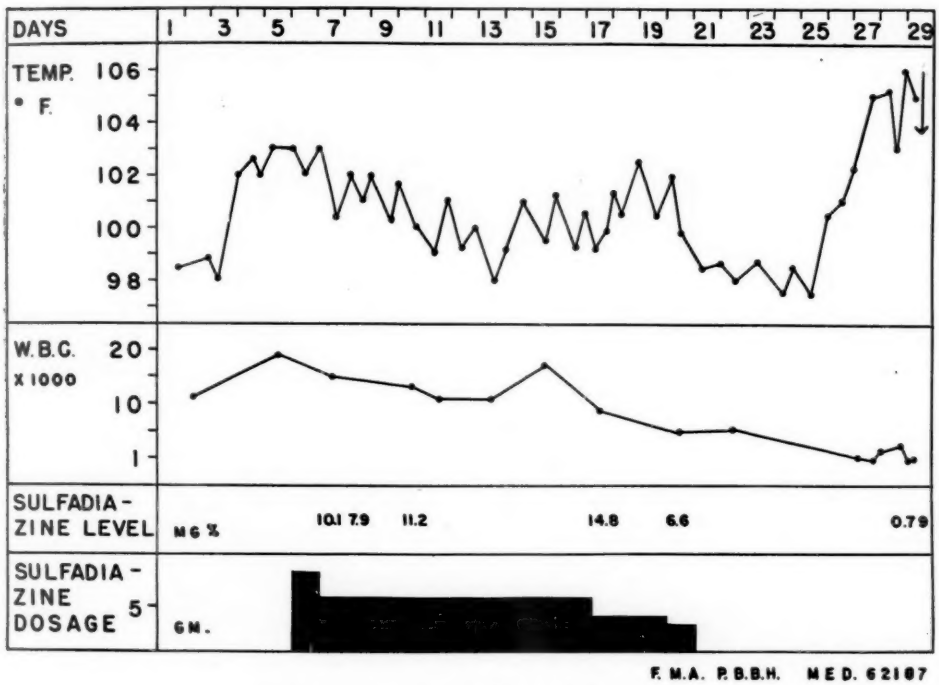

FIGURE 5. *Clinical Course of Case 8.*

C. *Administration to hospital and bed patients (large doses)*:

1. Instruct patient or nurse about importance of regular doses.
2. Measure urine output in 12-hour lots; perform a urinalysis daily during the acute phase.
3. Watch the temperature chart.
4. Determine the hemoglobin level weekly and the white-cell count three times a week; examine a smear weekly.
5. Examine patient daily, noting conjunctivas (pallor), skin (rash, purpura), scleras (jaundice), general appearance and behavior.

VIII. What should be done if a toxic reaction occurs?

Acute hemolytic anemia, purpura, hepatitis, high fever, severe rash and leukopenia are indications for immediate cessation of chemotherapy. Oliguria is an indication for omitting one or two doses until an adequate output returns. Following oliguria and particularly anuria, the renal function is apt to be somewhat impaired, so that the blood level should be watched more closely if the drug is readministered. In all toxic reactions the first move after discontinuing the drug should be the administration of a large amount of fluid (6 liters a day), to hasten the excretion of the sulfonamide. If evidences of infection return with the cessation of chemotherapy, several courses are open to the physician. First, do nothing if the infection is mild. Second, when the infection is severe, use serum or some other type of therapy if it is available. Third, try a different member of the sulfonamide group, using a 0.5-gm. trial dose and allowing twelve hours to elapse if possible. No adequate figures are available on the frequency with which reactions occur with the other sulfonamides if a toxic reaction occurs with one of them. In some cases it is possible to change from sulfathiazole to sulfadiazine (Case 7) without having any trouble. In other cases sensitivity to one member of the group seems to be associated with sensitivity to some or all of the others.

The treatment of agranulocytosis is very unsatisfactory. All that can be done is to force fluids to promote excretion, and to give large intramuscular injections of Pentnucleotide and crude liver extract, both of which may increase the white-cell count either by a stimulation of white-cell production or by maturation. Transfusion is relatively ineffectual, since a single granulocyte has a short

life, and some observers think that repeated transfusions may depress the bone marrow.

If anuria occurs as a result of sulfonamide therapy, fluids should be forced, and sufficient sodium bicarbonate given to bring the blood-bicarbonate level to normal if it is depressed. If no urine appears as a result of these measures, the ureters should be catheterized and lavage with mildly alkaline solution given as high as possible to dissolve and break up any calculi or precipitates in the ureters and pelves. This has been more successful with sulfapyridine than with sulfathiazole, which is apt to produce more damage in the kidney itself.

Summary

The following directions are suggested in sulfonamide therapy:

Do not give sulfonamides without good indications.

Do not withhold sulfonamides from desperately ill patients with undiagnosed infections.

If sulfonamide therapy is elected, use adequate doses.

If a patient is very seriously ill, begin with an initial intravenous dose of the sodium salt of the sulfonamide to be used.

Try to cure the patient in the first few days before toxic reactions confuse the issue.

Continue therapy for two or three days after all evidences of active infection subside, or until adequate localization occurs. In meningitis and deep infections involving bone, chemotherapy should be continued longer after apparent cure.

If no response to therapy occurs in two days, check the diagnosis, check the sulfonamide blood level, look for pus, and suspect drug fever.

If no response occurs to *adequate* therapy in three days, discontinue the drug.

Before administering sulfonamides, try to find out whether the patient has had them and had reactions previously.

Try to assess renal function before deciding on the dosage.

Watch for serious reactions, checking the white-cell count, particularly after ten days, and watching the urine output.

Continue to watch the white-cell count for a week after treatment is stopped.

Force fluids with all drugs but sulfonamide.

After the patient is cured, tell him which sulfonamide drug he has received; if he has had a reaction, instruct him to inform any physician about it before taking sulfonamides again.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28531

PRESENTATION OF CASE

A twenty-four-year-old nulliparous waitress entered the hospital complaining of abdominal pain of two weeks' duration.

One year before entry the patient had a two weeks' episode of pain in the right and left lower quadrants without chills, fever, nausea or vomiting. She was treated at a community hospital for five days with hot douches, and was apparently cured. She was perfectly well until two weeks before entry when she suddenly experienced throbbing pain in the left lower quadrant of the abdomen. The pain was not severe enough to double her up, but it persisted steadily for six days and then abated somewhat. On the third day of this attack her physician found that she had a temperature of 101°F., and gave her "large white pills," of which she took two every four hours for five days. The drug was stopped because of nausea and vomiting. Four days before entry she had an exacerbation of the pain, which continued until admission. She had had no gastrointestinal or genitourinary symptoms. She had lost about 15 pounds in the previous two months. Her last menstrual period had begun just after the onset of the pain.

She had had the usual childhood diseases. When eight years old she spent a year at a tuberculosis sanatorium because of a "swollen belly." She had several abdominal paracenteses there, and was told that her trouble was due to drinking unpasteurized milk. She had had an appendectomy four years before entry, and an operation for elephantiasis three years before.

She was married when eighteen years old and was separated eighteen months later, but admitted sexual intercourse since then.

Physical examination showed an obese woman with five operative scars, two in each thigh and one in the right lower quadrant. Examination of the heart and lungs was negative. The lower abdomen was prominent, especially on the left, where there was marked tenderness with questionable spasm. There was no tympany, and peristalsis was normal. There was a large rounded lower abdominal mass, which seemed to reach to the umbilicus. The liver was felt one finger-breadth below the right costal margin. The spleen was not palpable. Pelvic examination showed a marital introitus, slight leukorrhea and a normal nulliparous nontender cervix. There was marked tenderness in both vaults, and the fundus could not be felt because of the extreme tenderness. The abdominal mass was tender and did not seem to be connected with the cervix. Rectal examination confirmed the vaginal findings.

The temperature was 100°F., the pulse 64, and the respirations 20. The blood pressure was 96 systolic, 52 diastolic.

Examination of the urine was negative except that the sediment showed 15 to 20 white cells per high-power field; a culture was negative. The blood showed a red-cell count of 4,700,000 with a hemoglobin of 90 per cent, and a white-cell count of 8800 with 76 per cent polymorphonuclears. A cervical smear was negative for gonococci. A blood Hinton test was negative. A tuberculin test (1:100,000) showed a 3-cm. area of erythema at the end of forty-eight hours. An Aschheim-Zondek test was negative.

An abdominal roentgenogram showed a huge soft-tissue mass in the abdomen rising to the level of the first lumbar vertebra and swinging to the left. There was an indefinite area of calcification overlying the left side of the fourth lumbar vertebra, and a similar indistinct area of calcification overlying the left twelfth rib. The areas of calcification appeared to lie peripherally about the mass. An intravenous pyelogram was negative. The mottled calcification seemed to lie over the upper pole of the left kidney but was shown to shift its position relative to the kidney calyxes. The bladder film showed a pressure defect that almost obliterated the left half of the bladder. Following a barium enema, the sigmoid was seen to be displaced and plastered against the abdominal mass.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. GRANTLEY W. TAYLOR: We are concerned with a young woman who presented a large abdominal tumor that had given rise to symptoms of only two weeks' duration.

The past history almost certainly establishes that she had tuberculous peritonitis in childhood, from which she apparently recovered completely. A

laparotomy for appendicitis four years previously would presumably have disclosed persistent disease if it had been present, and might also have revealed the tumor if it had been of long standing. Nothing is offered regarding a possible explanation for the development of elephantiasis in a woman who required operation at the age of twenty-one. In this connection it would be of interest to know her race and nativity. It must be assumed that at some time she suffered from a thrombophlebitis resulting in obliteration of the lymphatic pathways. This may have occurred during her hospitalization in childhood, or possibly following her appendectomy. A year before admission she had an episode of lower abdominal pain, which was probably due to an acute pelvic inflammation.

It is difficult to picture that any of these previous illnesses had any bearing on the tumor. Tuberculosis may give rise to large lymph nodes or inflammatory masses in the abdomen, and these may be associated with calcification, as shown in the x-ray films. But if these had occurred, symptoms would undoubtedly have been present over a longer period, and it would be most unusual for such a large mass to have been present. It is conceivable that a pelvic tumor by pressure could have given rise to the elephantiasis of the thighs, but under these circumstances there would have been numerous other related symptoms. Very large pus tubes may sometimes follow acute pelvic inflammation, but they never achieve the size of this tumor and would undoubtedly present more symptoms in the course of their development.

Other types of inflammatory masses in the abdomen might be mentioned, such as a large hydronephrosis or pyonephrosis and the inflammation surrounding diverticulitis of the sigmoid, but there were no other signs and symptoms suggesting the presence of such conditions.

May we have the x-ray films?

DR. JAMES R. LINGLEY: This mass is very large, filling the lower abdomen and extending out to the left flank. It is uniform in density throughout and has sharply defined, smoothly rounded borders without lobulation. It displaces the sigmoid medially but does not involve the bowel.

There are at least six areas of calcification in the abdomen, all of which lie outside the large mass. The four in the upper abdomen have the typical appearance of calcified mesenteric tuberculous lymph nodes. The lower two, however, are unusual in two respects, if they are nodes. First, their positions are wrong, as one lies well out in the right flank and the other lies anteriorly immediately against the anterior abdominal wall. Secondly, their density is uniform throughout and is much less than one expects in a tuberculous node. Their density and structure suggest the calcification sometimes seen in a certain tumor that occasionally involves the peritoneum extensively.

The film of the chest shows normal lungs, but the diaphragm is elevated, particularly on the right.

DR. TAYLOR: Are the psoas muscles normal?

DR. LINGLEY: Yes; and the kidneys and ureters are not remarkable.

DR. TAYLOR: By x-ray the area of mottled calcification was said to move independently of the kidney, and there were no symptoms referable to the genitourinary or gastrointestinal tract.

An echinococcus cyst must be mentioned as a possibility. Again knowledge of the race and nativity of the patient would be helpful. No specific tests were carried out. Presumably an eosinophilia would have been noted in the blood smear if it had been present.

When we come to consider the various cysts and tumors that may occur in the abdomen, we are at once impressed with the silent character of the tumor prior to the acute episode. The position of the tumor in relation to the side of the bladder, as shown by the x-ray films, argues for a pelvic origin, rather than a tumor involving the liver, spleen or kidney. A cyst of the mesentery or omentum may be present in the pelvis, but does not result in the lower abdominal and vault tenderness. Fibroids and ovarian and paraovarian tumors and cysts are the most likely masses to consider.

Regarding a fibroid tumor, the patient was young, the mass seemed independent of the cervix, and there was no abnormal menstrual history. These do not necessarily rule out fibroid, but tend to. Between solid and cystic ovarian masses, the large size of the tumor argues for a cyst, as does the absence of early symptoms of pressure.

An explanation of the acute episode, with pain, fever and tenderness, must be offered. It seems probable that there had been some torsion or interference with the blood supply to explain these symptoms. In my opinion, the preoperative diagnosis is ovarian cyst, with a torsion of the pedicle. The areas of calcification shown in the x-ray films may have been residuums from the old abdominal tuberculosis, or they may have been areas of calcification in the cyst itself.

DR. LINGLEY: I do not believe that all the calcification is typical of either calcified tuberculous mesenteric nodes or of the tumor I mentioned, namely, papillary cystadenocarcinoma of the ovary. It is quite possible that all the calcification is tuberculous in nature, but in view of the large mass, which is probably a cyst of the ovary, I suggest that the entire picture may have been due to papil-

lary cystadenocarcinoma of the ovary, with extensive psammoma calcification throughout the abdomen. I should be much happier about the latter diagnosis if there were psammoma calcification within the large mass itself.

DR. LOWREY F. DAVENPORT: What about the palpable liver?

DR. TAYLOR: I do not believe that is significant in the presence of obesity.

DR. CLAUDE E. WELCH: I should cast doubt on the past history of elephantiasis, inasmuch as only the thighs were involved.

DR. JOHN H. TALBOTT: I should like to offer one diagnosis that probably does not contribute to the principal difficulty in this patient. The past history of tuberculosis, the presence of hypotension and the roentgenograms of the abdomen showing calcification over the upper pole of the right kidney make one consider Addison's disease. If I had seen only the plain films of the kidney, both anteroposterior and lateral, I should have called it typical of calcified adrenal tissue and highly suggestive of Addison's disease. Of course in consideration of the entire picture one is foolish to make a diagnosis of Addison's disease, but I do believe that the patient is a likely candidate for that disease in the future. She may well develop a lesion of the left adrenal gland in addition to that of the right, which is demonstrable now.

DR. LINGLEY: I agree that there is one small area of calcification in the region of the right adrenal gland, but I doubt that it is in the gland since it moves independently of the kidney, and in the lateral view lies anterior to it.

DR. ALFRED KRANES: Should a mesonephroma be considered?

DR. LINGLEY: I am not familiar with that condition.

DR. DONALD S. KING: Could this be a tuberculous mass?

DR. TAYLOR: I have never seen a tuberculous mass reach this size.

DR. JAMES H. TOWNSEND: I believe that tuberculous salpingitis can sometimes result in the formation of a mass of this magnitude.

CLINICAL DIAGNOSIS

Ovarian cyst.

DR. TAYLOR'S DIAGNOSES

Ovarian tumor, probably a cyst, with torsion.
Old tuberculous peritonitis.

ANATOMICAL DIAGNOSES

(Pseudomucinous cyst of ovary.)
Encapsulated tuberculous peritonitis with calcification.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on by Dr. Burbank, and I shall ask him to describe his findings.

DR. CHARLES B. BURBANK: Our preoperative diagnosis was ovarian cyst. At the time of operation about 2500 cc. of clear yellow fluid under some pressure was found free in the peritoneal cavity. The entire lower abdomen was filled with a large cystic mass, which was adherent to the anterior abdominal wall at the level of the symphysis pubis and also to the right iliac fossa. On the other side it extended almost to the left iliac fossa. Its upper border was at the level of the umbilicus. It had pushed the small intestine forward, and many coils of the ileum were adherent to its anterior and lateral walls and also to each other. It was impossible to enter the pelvis or to identify any of the pelvic organs. Lying just below the peritoneum at the upper end of the incision was a separate mass, measuring 5 by 4 by 2 cm., with a yellow surface. It was soft in consistence and when opened contained white material suggestive of tooth paste. This was totally excised.

Since it was obviously impossible to free up the large cyst, the wisest procedure appeared to be to drain it through the abdominal wall. When an incision was made into it, a large amount of clear fluid was evacuated. A segment of the wall was removed. The inner surface of the cyst was smooth. It was my impression that it was a pseudomucinous cyst, presumably of the right ovary.

DR. MALLORY: In none of the material submitted to the laboratory could we positively identify the cyst as ovarian in origin. However, I think Dr. Burbank's impression can be accepted with reasonable confidence. The smaller mass proved to be an encapsulated mass of semicaseous exudate with active tubercle formation in some portions of its wall and many foci of calcification, 50 to 200 mm. in diameter, in other areas. Many of these were not larger than psammoma bodies, so it is natural that the x-ray picture should have suggested an ovarian papillary cystadenoma to Dr. Lingley.

CASE 28532

PRESENTATION OF CASE

A twenty-one-year-old girl entered the hospital complaining of chills and fever of two and a half weeks' duration.

At nine months of age the patient had been seen at another hospital because of fever and vomiting. The outstanding and relevant findings at this time

were a temperature of 103°F., a pulse of 190 and a respiratory rate of 60. The heart was markedly enlarged to the left with a blowing systolic murmur all over the precordium, but heard best at the apex and transmitted to the back; the enlargement was verified by x-ray examination. At the end of a month the heart had decreased in size, the left border being only 6.5 cm. from the midsternal line, with the apex in the fifth interspace. She was discharged two days later with a normal temperature and respirations, but the cardiac murmur had persisted. The patient was readmitted to the above institution two months later with a temperature of 102°F., and a pulse of 150. The same cardiac findings were recorded, the left heart border varying from 8.5 to 9.5 cm. from the midsternal line. No significant signs were noted in the lungs, nor was there clubbing of the fingers. During the next two years the patient was examined in the outpatient department of the same hospital at infrequent intervals. The same cardiac abnormalities were noted, and during this period she suffered from urticaria, nasopharyngitis and tonsillitis, the last of these being eliminated by an adenotonsillectomy.

At the age of sixteen, the patient was first seen in the Cardiac Clinic of the Out Patient Department of this hospital, and she continued her visits until the time of admission. No history of rheumatic fever could ever be obtained, and the patient denied having had sore throats, joint pain, chorea, fever, nosebleeds, dyspnea and cardiac arrhythmia, although she suffered from about three head colds each year. The following is a summary of the findings during this period. The patient's appearance was always rather delicate and sickly. The heart was markedly enlarged, the impulse heaving, without a palpable thrill, and the rhythm regular at a rate averaging 100. The sounds were tumultuous, with a loud systolic murmur at the apex replacing the first sound and transmitted to the left lung base. During these years an apical mid-diastolic murmur was thought to be present by some examiners, usually brought out by exercise. The blood pressure averaged 95 systolic, 75 diastolic. Occasionally rhonchi were heard at the lung bases, but at no time were there subcutaneous nodules, clubbing of the fingers or a palpable spleen; a tendency to cyanosis after exercise was very questionable. Three years before admission an x-ray film of the chest showed a heart that was grossly abnormal in shape, with an unusually prominent left upper border. The aorta was small, and the pulmonary vessels dilated. The peripheral lung fields were clear, and the diaphragm was low. Another x-ray examination two years later showed that the heart was enlarged to the left as well as in the anteroposterior diameter, with a questionable enlargement of the left auricle. The pulmonary conus was prominent, and the hilar vessels and vessels within the lung parenchyma were wider than usual. Fluoroscopy was performed six months before admission and showed enlargement of both the right and left ventricles, with a cardiothoracic ratio of 12:19. The pulmonary conus was enlarged, and a considerable degree of pulsation was seen in the pulmonary arteries. There was no significant enlargement of the auricles. An electrocardiogram at this time showed normal rhythm, a rate of 90 and a PR interval of 0.19 second. T_3 was flat; the QRS voltage was unusually high in Leads 2 and 3, and its amplitude widened to 0.12 second. There was no abnormal axis deviation.

During all this time the patient led a quiet life and remained fairly well, although she entered the hospital for six days on one occasion suffering from severe gingivitis, which cleared readily on treatment.

Two and a half weeks before entry the patient "caught cold"; the onset was accompanied by malaise, anorexia, a persistent cough and chills, and was followed by a low-grade fever. She went to bed and during the next three days had several more chills; at the end of this period, however, the temperature fell to normal and she felt better. The patient resumed her usual activities, but one week before admission a severe chill occurred, which was followed by a temperature varying from 99 to 104°F. In bed again, she suffered from a series of shaking chills with occasional night sweats, and thirty-six hours before entry, at four o'clock in the morning, a severe chest pain awakened her from sleep. This pain was sharp, located in the right chest posteriorly, was aggravated by deep breathing and coughing, gradually increased, but was relieved somewhat by hot packs.

The patient's mother had had rheumatic fever and tuberculosis, and one sister had tuberculosis of the spine.

On examination, the patient was thin, poorly developed and appeared chronically ill, with pale, shiny skin, slight mucous-membrane cyanosis, slight clubbing of the fingers with floating nails and a definite increase in the volume of the jugular pulse. Examination of the head and neck was negative. The lungs were clear. The heart was enlarged, the border being 1.5 cm. to the right of the midsternal line with the apex palpable at the anterior axillary line in the sixth intercostal space. The apex impulse was rapid, regular and forceful; no thrills could be felt. There were two low-pitched murmurs at the apex,—a loud systolic and a rumbling diastolic,—the former being

transmitted to the left lung base. In addition, a high-pitched and loud systolic and a short mid-diastolic murmur were heard just to the left of the lower sternum. These last two murmurs were rather distinctive, but could not be separated definitely from those at the apex. The liver was just palpable, and the spleen easily palpable. Vaginal and rectal examinations were negative.

The blood pressure was 95 systolic, 65 diastolic. The temperature varied between 99 and 105°F. The pulse averaged 100, and the respirations 27.

Examination of the urine was negative. The blood showed a red-cell count of 4,300,000 with a hemoglobin of 13 gm. and a white-cell count varying between 9000 and 18,000, of which 75 per cent were polymorphonuclear leukocytes. Repeated blood cultures yielded Type 6 pneumococci. The nonprotein nitrogen of the blood serum was 26 mg. per 100 cc. The blood Hinton reaction was negative. The stools were normal.

An electrocardiogram showed a normal rhythm with a rate of 115 and a PR interval of 0.20 second. The QRS complex in Leads 2 and 3 was M shaped and low.

An x-ray film of the chest showed gross cardiac enlargement, apparently in the region of the right ventricle and pulmonary artery. Also, there was slight dilatation of both auricles. The aorta was unusually small, whereas the pulmonary vascular shadows were increased in number and size. There were no areas of consolidation in the lungs, and no fluid at the bases. Fluoroscopically, a hilar "dance" was noticed.

Throughout the patient's illness chemotherapy was used, starting with sulfadiazine, which reached a blood level averaging 12 mg. per 100 cc. However, by the thirteenth hospital day, this level had climbed to 21.2 mg. so the drug was discontinued, and the next day the concentration dropped to 15.9 mg. During the last few days of life a shift from sulfadiazine to sulfathiazole was made because the patient had failed to respond to the former drug.

The first few days of hospitalization were without incident, but six days after admission the patient developed a headache, but remained clear and co-operative. Examination showed a widely dilated left pupil, which failed to react, and a third-nerve paralysis on the left, the patient being unable to open the eyelid. A lumbar puncture revealed no abnormalities. She was given 100,000 units of Type 6 antipneumococcus rabbit serum intravenously in four hours, after a negative Francis test. The next day an additional 60,000 units was administered. Four days later the patient developed slight weakness of the seventh left cranial nerve, with a slightly stiff neck and a positive Kernig sign. Two weeks after admission, pain on respiration developed in the right lower chest anteriorly, with slight cough and dyspnea but no sputum. Examination revealed a few rales and a slight rub low in the right axilla at the end of inspiration. Death occurred on the eighteenth hospital day after an increase in cyanosis and the development of puffiness of the face and moist rales bilaterally. Bronchovesicular breathing with increased whispered voice sounds was heard over an area 4 cm. in diameter at the left lung base.

Differential Diagnosis

Dr. Edward F. Bland: First I should like to ask Dr. Sullivan to comment on the Francis test and its significance.

Dr. Eugene R. Sullivan: The Francis test depends on the reaction between the type-specific soluble carbohydrate extracted from the capsule of the pneumococcus and its corresponding antiserum. By injecting intradermally a small amount of the specific carbohydrate (in this case, Type 6), one can test for the presence in the blood of Type 6 pneumococcus antibodies, either of natural development or artificially administered. A positive skin reaction is frequently used as a guide to indicate that enough antiserum has been given.

Dr. Bland: There are two diagnostic problems presented by this case: the answer to the first is evident, but that to the second is difficult.

In connection with the first, the clinical course indicates clearly that this patient succumbed to a pneumococcal septicemia associated with acute bacterial endocarditis superimposed upon previously existing heart disease and complicated by pulmonary infarcts (presumably septic) and by either a metastatic brain abscess or meningitis — probably a combination of the two. A special feature of the embolic phenomena will be commented on later, since it may prove helpful in trying to unravel the second, and more difficult, feature of the case — namely, the underlying type of cardiac disease and especially the structural defects present within the heart.

Any patient in the vicinity of Boston with chronic heart disease in this age group deserves, first, a most careful scrutiny for evidence of rheumatic heart disease, since in this part of the world rheumatic fever is responsible for more than 95 per cent of the crippled hearts in young people. However, I do not believe in this case we have sufficient evidence to consider seriously this etiologic factor. In the first place, the existence of heart disease was recognized at the age of nine months. This is unusually early for the onset of rheumatic fever, although rare cases have been recorded even

in infancy. The youngest patient I have personally observed with rheumatic fever was fourteen months old. The absence of an illness recognizable as rheumatic fever in this patient is only moderately helpful in a negative direction. Of considerably more importance in excluding a rheumatic factor, I believe, are the physical signs, which are not in accord with the more or less well-defined pattern presented by chronic rheumatic scarring of either the mitral or of the aortic valve, and the appearance of the electrocardiogram, which in this instance is particularly suggestive, not of rheumatic heart disease, but of a congenital cardiovascular defect. On these grounds I am therefore willing to discard rheumatic heart disease from further consideration.

I believe we are concerned with a congenital defect in the heart, possibly a combination of such defects. The problem is to name the condition, for we no longer consider it adequate to dismiss such cases with the broadly inclusive term of "congenital heart disease." Experience has shown that an accurate structural diagnosis is possible in the majority of those who survive the first few months of life. A definitive diagnosis in these cases is of considerably more than academic interest for it determines within limits the prognosis, and in an occasional case leads to corrective surgery.

May we have an interpretation of the x-ray films at this point? I notice from the dates that the films submitted are those taken approximately six months before death, when the patient was in relatively good health. The films taken during the final illness are, unfortunately, not available.

Dr. James R. Lingley: The films taken six months before death show clear lung fields. The heart shadow is grossly abnormal in size and shape. The enlargement is predominantly ventricular, and it appears to affect the right side more than the left. The aorta is hypoplastic as shown by the absence of the curve of the ascending portion along the right upper mediastinum and by the inconspicuous knob. The pulmonary conus is very prominent, and the pulmonary artery is dilated. There is also dilatation of the vascular shadows throughout both lungs, and fluoroscopically a hilar "dance" was demonstrated. So far as I know, this occurs only in congenital heart disease, and most commonly in association with a patent ductus arteriosus or an interauricular septal defect.

Dr. Bland: To me these films indicate primarily three things: prominence of both the right and left ventricles — this is supported by the absence of either right-axis or left-axis deviation in the electrocardiogram and hence relatively little disproportion between the two ventricles; little or no enlargement of the auricles; and a striking increase in the amount of blood in the pulmonary circulation.

These findings suggest a shunt within (or near) the heart. If my major premise is correct, namely, that we are dealing with a congenital heart, then the absence of cyanosis (except of slight extent terminally) indicates that the shunt involves a flow of blood from the left (arterial) to the right (venous) side of the heart. This in turn would explain the dense vascular shadows in the lung roots, and the later pulmonary signs (infarcts).

In regard to the location of the shunt, there are three possibilities. The first is a patent ductus arteriosus, which I am inclined quickly to exclude because of the absence of the characteristic physical signs and no widening of the systemic pulse pressure. The second is a large interauricular septal defect, which with some hesitation I am also willing to discard, at least as the major anomaly, largely because of the absence of x-ray evidence of right auricular enlargement, and also because of the absence of right-axis deviation in the electrocardiogram. The third possibility, a defective interventricular septum, seems to me by far the most likely diagnosis. To be sure the murmurs described do not accord with the classic midsternal systolic murmur accompanying septal defects that are small, that is, less than 1 cm. in diameter. In this case, however, I should expect a large defect to be present because of the cardiac enlargement, the large amount of blood in the pulmonary circulation, and especially the appearance of the electrocardiogram. The last, as you recall, showed a wide amplitude of the QRS complexes in Leads 2 and 3, with unusually prominent and deep S waves together with a slight degree of intraventricular block. In fact, this electrocardiogram is so strikingly similar to that of a boy with a single ventricle whom we studied in this hospital about ten years ago that I am tempted to suggest that rare possibility in this case.

A word remains to be said about the final illness. Patients with congenital defects, especially of the interventricular septum, frequently succumb to superimposed bacterial endocarditis, most often subacute in nature and caused by *Streptococcus viridans*. Less often this infection is due to *Str. haemolyticus*, *Staphylococcus aureus* or a pneumococcus, in that order of frequency, and if so, the course is more acute — two to six weeks. Since the abnormal flow of blood is from left to right in the heart, it should be remembered, emboli are swept backward into the pulmonary circulation, with resulting infarction in the lungs. This is my interpretation of the intermittent acute pulmonary symptoms of which this patient com-

plained and which toward the end were associated with signs of pulmonary consolidation.

How are we to explain the cerebral symptoms? Was this a paradoxical embolus toward the end as the pressure gradient between the two ventricles declined, and the pulmonary circulation became more engorged? Or was there in addition a complicating interauricular septal defect that permitted passage of an embolus under similar circumstances? I do not know, but I think a more likely explanation is extension of the bacterial vegetations into the left side of the heart with resultant peripheral emboli. Perhaps there was meningitis secondary to the septicemia per se.

To summarize briefly, I believe this patient had congenital heart disease — a large interventricular septal defect (essentially a single ventricle) — and acute bacterial endocarditis, predominantly in the right side of the heart, involving the defect and almost certainly the adjacent cusps of the tricuspid valve with septic infarcts in the lungs and probably in the brain, associated with meningitis. Dr. Heyl, would you comment on the neurologic aspects of the case?

Dr. Henry L. Heyl: The significance of a unilateral third-nerve palsy is often obscure. It could represent a local lesion in the region of the nucleus, such as infarct, abscess or thrombosis. It could be caused by a local meningitis secondary to the bacteremia. It might even be due to a contralateral mass pushing the brain to the left and catching the nerve between the tentorium and the cerebral peduncle. Of all these, the presence of a local meningitis seems most likely in this case, with or without a small, precisely placed infarct in the region of the third-nerve nucleus. The appearance of the seventh-nerve palsy may have represented a spread of infection or a repetition of infarction; however, it was more likely a nonspecific cerebral manifestation of terminal disease.

Dr. James H. Townsend: Would you comment on what you consider the most important signs in patent ductus arteriosus?

Dr. Bland: A continuous murmur to the left of the upper sternum usually accompanied by a systolic thrill.

Dr. S. Peter Sarris: Can pulmonary regurgitation give a hilar "dance"?

Dr. Bland: Yes; but organic pulmonary regurgitation is extremely rare.

Clinical Diagnoses

Congenital heart disease (? cor triloculare).
Acute bacterial endocarditis (Type 6 pneumococcus).
Acute meningitis (Type 6 pneumococcus).
Bronchopneumonia.

Dr. Bland's Diagnoses

Congenital heart disease: interventricular septal defect large (? cor triloculare, with a single ventricle).
Acute bacterial endocarditis (Type 6 pneumococcus, involving septal defect and tricuspid valve.
Infarcts, septic: lungs and ? brain.
Meningitis.

Anatomical Diagnoses

Congenital heart disease: interventricular septal defect, very large (cor triloculare biatriatum).
Bacterial endocarditis, subacute, tricuspid (Type 6 pneumococcus).
Endocarditis, chronic, tricuspid.
Pulmonary embolism, multiple.
Dilatation of pulmonary artery.
Hypoplasia of aorta.
Cardiac hypertrophy.
Pulmonary edema.
Hydrothorax.
Infarcts of lung, spleen and kidneys.
Hypertrophic pulmonary osteoarthropathy, minimal.

Pathological Discussion

Dr. Tracy B. Mallory: The first suggestion that this patient was suffering from congenital heart disease came from Dr. Schatzki, following x-ray examination. Before that time everyone had accepted the diagnosis of mitral stenosis. When the cardiologists were called in consultation they, too, were inclined to congenital heart disease, Dr. Ashton Graybiel favoring an interatrial septal defect and Dr. P. D. White an interventricular one. In fact Dr. White, whose note I shall read, hit the nail directly on the head like Dr. Bland, by suggesting a triloculate heart with a single ventricle.

> This is an acute type of bacterial endocarditis not responding to chemotherapy as yet. The problem concerns the diagnosis of the underlying heart disease. Certainly the findings do not fit any of the ordinary types of congenital heart defects, such as patent ductus, ventricular septal defect, auricular septal defect, coarctation of the aorta, tetralogy of Fallot and aortic or subaortic stenosis; and yet the early age at which the heart disease was discovered (nine months), the bizarre electrocardiogram (wide QRS waves with very prominent R and S deflections in Leads 2 and 3) and odd x-ray picture support the diagnosis of congenital heart disease. Because of the similarity in certain respects (electrocardiographic murmurs and terminal cyanosis) with our one case of triloculate heart with a single ventricle I should hazard that diagnosis here. The next best bet is a very unusual rheumatic heart with early development of mitral and perhaps also

tricuspid stenosis (such valve defects are also possible but very improbable as congenital lesions).

The murmurs are a low-pitched but fairly loud systolic and a rumbling diastolic at the apex, the former transmitted to the left lung base and undoubtedly mitral in origin, and a considerably higher pitched and also fairly loud systolic and a short mid-diastolic at the left of the lower sternum (the last-named murmurs sound rather distinctive but cannot actually be separated from the apical murmurs, whence they may be transmitted; I do not think they are pulmonary or aortic in origin, but they might be tricuspid).

The jugular pulse is distinctly increased and the liver is a bit down, both of which are indicative of congestive heart failure.

The prognosis is, I fear, hopeless.

The post-mortem examination showed a normal interauricular septum with a completely closed foramen ovale. In contrast, only rudiments of an interventricular septum were present and there was essentially but one ventricle. Both the tricuspid and mitral orifices opened into this. The tricuspid orifice showed a valve with only two, instead of the usual three, leaflets and the chordae tendineae and papillary muscles were correspondingly abnormal. The margins of the tricuspid valve were thick and fibrous, indicating an old healed endocarditis almost certainly rheumatic in type. On one of the two leaflets was a large bacterial vegetation. The pulmonary artery was extremely large, and the aorta relatively small. The coronary arteries were normal. Within the lungs the pulmonary branches showed extensive atheroma. Three infarcts were present in the lungs — a large one, 5 by 4 by 3 cm. in the right upper lobe, another large one 5 cm. in diameter in the base of the right lower lobe and a smaller one 2 cm. in diameter also in the right lower lobe. Fresh emboli were found in the corresponding branches of the pulmonary artery. The liver showed moderate chronic passive congestion. The spleen weighed 350 gm., and one infarct was present in the kidneys.

DR. BLAND: Was the central nervous system examined pathologically?

DR. MALLORY: No.

DR. M. B. HARRISON: I have one comment to make. In looking over the very few electrocardiograms of triloculate hearts that are available, Dr. White pointed out a similarity, in that there was an unusually high voltage and wide swing of the QRS complex in Leads 2 and 3 without abnormal axis deviation. Although the diagnosis of triloculate heart is hardly ever made during life, this finding in the electrocardiogram may be a definite clue in future cases, as it proved to be here.

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The Journal does not hold itself responsible for statements made by any contributor.

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1943

Another New Year is making its bow on the horizon, and when we express the hope that it will be a "happy" one for our readers, their uncles, their cousins and their aunts, we are using the adjective in a broad sense. The year will certainly not maintain a high level of hilarious gaiety for any of us, and too great a degree of personal comfort will hardly be considered as consistent with common decency. It will bring hardships and disappointments and, for many, great sorrow, and it will contain anxious days, and hours, perhaps, of frank discouragement.

What we can hope, however, is that to all of us as individuals will come the satisfaction — call it happiness if you will — that results from the fulfillment of our obligations, whether they are met at home or afield, in hospital or at the scene of action. And when the year draws to its close will come the gratification of knowing that we are another twelve months nearer to victory and to ultimate peace.

May this year bring to us also a clearer conception of the goal for which we are striving so that we may recognize it as being worthy of our struggle and our sacrifices, and may it certainly include the extension of our own bill of rights to the little people of all nations — all races, all creeds and all colors.

And as we make our sacrifices, small or great, let us not lay undue stress on them, for may we also remember the ancient sacrifice that still stands — "a humble and a contrite heart."

BOSTON'S HEALTH UNITS

In view of the recent gathering for the celebration of Charles F. Wilinsky's sixtieth birthday, it is appropriate to call attention to one of his outstanding contributions to community welfare — the Boston health units.

At Pittsburg, in 1915, a "health center" for tuberculous patients was established. News of it set in motion a train of thought in the mind of Dr. Wilinsky that ultimately led to his conception of the modern health unit. He promptly communicated his idea to the health commissioner of Boston, Dr. Francis X. Mahoney, and shortly thereafter Dr. Wilinsky and a small group of his friends met at the house of Dr. Richard C. Cabot to discuss the project. Dr. Wilinsky pointed out to the group the advantages that would result from co-operation and co-ordination of effort in each health district of Boston if the activities of official and voluntary health agencies could be brought together under one roof. Sensing the close relation between poverty and ill-health, he also proposed that the welfare agencies should be represented in the unit. Dr. Cabot approved the plan, and the Honorable James M. Curley, then mayor of Boston, was persuaded to adopt it.

The first health unit was opened on Blossom Street in 1916. Dr. Wilinsky, who was already an official of tl. Boston Health Department in charge of the West End Health District, became the director of the unit, and under his able leadership the project soon proved its value.

Although improved in succeeding years, the quarters of the unit, consisting of a hall that had been used for a ward-room and subsequently as a gymnasium, were totally inadequate, according to present-day standards. Furthermore, expansion of the program by the provision of additional units in congested districts was slow on account of the expense and of the opposition of those who were not sympathetic.

Dr. Wilinsky always stressed the point that the units should not duplicate the work of clinics. On the contrary, he believed that they should decentralize the services of the Health Department and make them more readily available to the public. Year after year, confidently and persistently, he explained the health-unit idea and gained additional supporters. He convinced the Mayor's Office, the Advisory Board of the Health Commissioner, the Boston Health League and several medical and other groups that had opposed him at first. But it was not until the trustees of the George Robert White Fund became interested in the program that fine buildings were constructed to house the units. The projected series of units was finally completed in 1933.

The fame of the health units has spread far and wide. They have been visited and admired not only by health officials from other American cities, but also by leading sanitarians from many of the countries of Europe. It can truly be said that from Dr. Wilinsky, more than from any other, came the vision, the energy and the enthusiasm that gave Boston these health units. With the passing years will come perspective by which their value can be accurately appraised. It seems likely, however, that they will ultimately be regarded as one of the greatest contributions of this generation to public-health administration.

MEDICAL EPONYM

Eustace Smith Sign

This sign, although not unanimously accepted as valid, is still frequently referred to. It was described by Dr. Eustace Smith (1835–1914), physician of the East London Children's Hospital, in a communication, entitled "On the Diagnosis of Enlarged Bronchial Glands in Children" (*Lancet*, 2: 240, 1875). He writes:

> The symptoms by which enlargement of the bronchial glands can be distinguished . . . are all pressure signs due to the encroachment of the swollen body upon the parts around. . . . At an earlier period, and before the enlargement has become . . . great, . . . much assistance can be gained from the following experiment. If the child be made to bend back the head so that his face becomes almost horizontal and the eyes look straight upwards at the ceiling above him, a venous hum, varying in intensity according to the size of the diseased glands, is heard with the stethoscope placed upon the upper bone of the sternum. As the chin is now slowly depressed, the hum becomes less loudly audible, and ceases some time before the head is brought back again into the ordinary position.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Analysis of Causes of Maternal Death in Massachusetts during 1941

Surgical Complications

Of the 10 deaths that resulted from surgical complications, 5 were due to appendicitis and peritonitis, 3 followed intestinal obstruction, and 2 were associated with ovarian cysts. There were two autopsies.

Of the 5 cases complicated by appendicitis and peritonitis, the first occurred in a primipara who at three months was operated on for symptoms of acute appendicitis of unstated duration. At operation the appendix was found to be ruptured and there was free pus in the abdominal cavity, because of which drains were left in the abdomen. General peritonitis resulted, and death occurred on the fifth postoperative day. The chief question is how long this patient suffered before operation. Too often the symptoms of appendicitis are not recognized, because of pregnancy, until rupture has occurred. Whether or not pregnancy exists, appendicitis should be treated surgically as soon as a diagnosis has been made, and the sooner an operation is performed, the less chance there is of fatal peritonitis.

The second patient, who had had one previous pregnancy, had what were described as "bearing-down pains" in the abdomen and nausea at five months. These complaints continued for two days, at the end of which time a threatened abortion was diagnosed. The following day the patient had a temperature of 100°F. and a rigid abdomen. A diagnosis of acute appendicitis was made, the patient was hospitalized, an unruptured appendix was removed, and the abdomen was drained. She was transfused two days later, and the following morning a spontaneous abortion occurred. Death followed in two days from peritonitis. It is possible that if a diagnosis of acute appendicitis had been made at the onset of this illness and operation performed immediately, this fatality might have been averted. The abortion following operation was probably due to the infection rather than to the operation itself. It must always be borne in mind that a pregnant woman may have acute appendicitis and that this condition demands immediate operation — the sooner this treatment is carried out, the surer one may be of recovery.

The third case occurred in a primipara who had been seen prenatally and who, at about five and a half months, complained of pain in her back, which followed a fall. The temperature and pulse were said to be normal. The following morning she was seen because of pain in the abdomen and a white-cell count of 25,000. An acute gangrenous appendix was removed; three days after the operation the patient miscarried, and she died of peritonitis on the eleventh postoperative day. It is, of course, quite likely that the pain in the back of which the patient complained, regardless of a normal temperature and pulse, was really due to a retrocecal appendix. It is unlikely in an adult that, with a white-cell count elevated to 25,000 and a gangrenous appendix, there were only a few hours of symptomatology. This again emphasizes the importance of early diagnosis of appendicitis.

The fourth patient was a primipara who was delivered at term of a normal living infant but died on the fifth post-partum day of peritonitis. No operation was performed, but an autopsy revealed a perforated gangrenous retrocecal appendix and peritonitis. This was a most regrettable death.

The fifth case was that of a patient who had had six previous pregnancies and was operated on at approximately the fifth month for what was thought to be an ovarian cyst. Operation revealed an acutely inflamed retrocecal appendix, which was removed. The patient's convalescence was febrile and associated with vomiting and distention. Ten days after the first operation the abdomen was again opened and a gangrenous cecum and pelvic abscess were found. The patient went steadily downhill and died two days after the second operation. The surgery in this case cannot be commended. Undoubtedly this was an entirely unnecessary death.

Three deaths were associated with intestinal obstruction. The first case was that of a patient, six months along in her second pregnancy, who became acutely ill with nausea, vomiting and abdominal pain. A diagnosis of intestinal grippe was made; the vomiting persisted, and the patient was hospitalized. Two days later labor started spontaneously and a dead fetus was delivered normally. She underwent no operation and died twelve hours after delivery. Undoubtedly this was a case of intestinal obstruction, and operation should have been performed early. Persistent vomiting and abdominal pain in a patient who is pregnant and without symptoms of toxemia should be considered indicative of an acute abdomen. The only way to operate successfully on acute intestinal obstruction is to operate early. This patient did not receive the most intelligent treatment.

The second patient, who had had a previous cesarean section, was again delivered by section in her third pregnancy. She was known to have a hernia in the old scar, and following operation she had attacks of abdominal pain, nausea and vomiting, for which Levine-tube treatment was instituted without relief. Death occurred on the fifth post-partum day, and autopsy revealed incarcerated loops of small intestine in the hernia. There is no excuse for this fatality. The diagnosis of intestinal obstruction should have been made earlier, and immediate operation should have been performed.

Of the third case in this group the history is inadequate. The patent was apparently delivered normally but died from peritonitis following intestinal obstruction, which was due to gangrene of the rectum.

Of the 2 deaths associated with ovarian cyst, the first occurred in a patient who was hospitalized because of evidence of salpingitis; in spite of a spiking temperature and a white-cell count of 24,000 she left the hospital against advice. Operation was performed one month later because of continued pain; a pyosalpinx was discovered, and considerable pus was evacuated. A right ovarian cyst was also found, which ruptured on attempted removal. In addition, there was a three to four months' pregnancy, which had not been suspected. Death occurred from peritonitis. Pregnancy occurring in a patient suffering from acute salpingitis is certainly very unusual. It is probable that, had the salpingitis been treated conservatively and operation deferred, this fatality would not have taken place.

The second patient, who was curetted for a spontaneous abortion at about two months, developed sudden pain in the abdomen as she was about to be discharged from the hospital. Immediate operation revealed internal abdominal hemorrhage. It is said that the hemorrhage came from a ruptured ovarian cyst on the right. The patient died within thirty-six hours of the operation from continued bleeding associated with oozing from the abdominal wall. It is probable that a ruptured ectopic pregnancy was the cause of the intra-abdominal bleeding.

The chief lesson to be deduced from these surgical deaths is, Pregnancy should never be allowed to obscure a proper diagnosis. Consultation should be held in any questionable case of abdominal symptomatology. Early diagnosis means early operation; early operation, in contrast to deferred operation, means recovery rather than fatality. The patient who is reported to have had salpingitis should in all probability never have been operated on. The questionable case of ruptured extrauterine pregnancy represents a fatality due to incorrect diagnosis.

SECRETARY'S OFFICE

The following letter appears to be of sufficient general interest and importance to warrant publication.

MICHAEL A. TIGHE, *Secretary*

* * *

Dear Dr. Tighe:

During the next twelve months 276 nurses are to be drawn from New England every month to enter the military services, which means that a total of 3312 nurses under forty years of age will be lost from our civilian services in this area by the end of the year; 140 a month will be drawn from Massachusetts alone. This is a large number, and in order to reach it, almost every eligible nurse who can possibly go will have to volunteer. If we can retain enough young instructors and supervisors to keep up the preparation of new nurses, we shall be very fortunate. For almost every other position, the nurses meligible for military service will have to fill in. The understanding and support of physicians in encouraging the eligible young nurse to answer the call (which is still voluntary) is much needed.

This will leave many vacancies in hospitals to be filled by *increased classes of student nurses*, which is one of the essential ways of keeping up hospital standards of care. Recruitment of student nurses for schools of nursing grows constantly more difficult, in competition with the WAVES and WAACs and well-paying industrial jobs. Our midyear (February, 1943) classes in Massachusetts alone need *1100 more applicants* to meet the quotas set. Connecticut needs 351; Rhode Island 71; Maine 302; New Hampshire 148; Vermont 127; according to quotas.

The supply of student nurses is the concern of physicians as well as nurses. Studies have shown that family physicians have marked influence in directing young women toward nursing as a career. That is why we are addressing this letter to you, hoping that it may reach many physicians who will give this campaign for student nurses their active support.

Several questions are inevitable, which the following may answer:

1. *Where can the applicant find out about accredited schools of nursing?*

   From the secretary of the state Nursing Council for War Service: in Massachusetts at 420 Boylston Street, Boston; in Connecticut at 252 Asylum Street, Hartford; in Rhode Island at 42 Weybosset Street, Providence; in Maine at 54 Saunders Street, Portland; in New Hampshire at Elliot Community Hospital, Keene; and in Vermont at 3 Nelson Street, Montpelier.

2. *What are the requirements for entrance?*

   A high-school diploma with better than medium grades in the academic or college-preparatory course, with a minimum age of eighteen years. Married students are now accepted in most schools.

3. *What are resources for financial aid for those unable to meet the costs of a three-year course?*

   The federal government has appropriated $3,500,000 for nursing education, part of which is available for scholarships to cover tuition and entrance expenses, uniforms, books and so forth. This fund is available to accredited schools of nursing in hospitals with daily averages of 90 to 100 patients, or to smaller schools affiliating with others to make a well-rounded course. Tuition costs range from nothing to several hundred dollars, but the average is $75.00.

   The Federation of Women's Clubs in all the states are undertaking aid to student nurses as one of their year's activities and will have scholarship funds for personal expenses for students.

   Both these funds are assigned through the directors of the schools of nursing, to whom the students should apply.

   Some schools will concentrate the instruction in the first two and a half years of training, paying the students for their services during the last six months.

4. *What is the future for these student nurses who now crowd the schools of nursing?*

   New positions will inevitably be available in the Army and Navy Nurse Corps after the war, if larger military forces are maintained, as seems likely. Greatly increased numbers will be needed in veterans' services.

   The field of public health, both in this country and in reconstruction in other lands, is due for expansion. Hospitals will again replace students with graduates after the war. Marriage will take its usual toll. The opportunities for the well-qualified nurse seem to be broadening. Some unemployment of the poorly equipped nurse will probably be unavoidable.

5. *What resources are available for the hospital that has no room for enlarged classes of student nurses?*

   The federal fund of $3,500,000 is available for extra subsistence, including housing, food and laun-

dry, for additional instructors and instructional facilities and for expansion of clinical experience through affiliation with other institutions. Hospitals with daily averages of 90 to 100 patients may qualify. Smaller ones may qualify through affiliation with other institutions and centralization of instructional facilities to form a well-rounded modern unit for nursing education. Application should be made to the United States Public Health Service. Full details have been sent to every hospital.

These are the facts. We need the co-operation of physicians in helping nursing to meet the demands of the military services for graduates, and the requirements of the hospitals for new students.

Yours very truly,

HELENE G. LEE, *Executive Secretary*
Massachusetts Nursing Council for War Service

420 Boylston Street
Boston

WAR ACTIVITIES

CIVILIAN DEFENSE

PLANS FOR MORTUARY SERVICE

The Medical Division of the United States Office of Civilian Defense has issued *Medical Division Bulletin No. 5: Emergency Mortuary Services*, presenting plans for the organization of this essential part of the casualty services.

The bulletin suggests that the local chief of Emergency Medical Service, in co-operation with the medical examiner or coroner, the chief of police, the health officer and representatives of the private funeral directors and cemeteries, plan for the following necessary services: location of morgue facilities; administration of these facilities; training of supplementary mortuary personnel; responsibility for collection and preparation of the dead for burial; rules for emergency issuance of death certificates and burial permits; types of inquests, if any, to be required; safeguarding of personal property of the dead; manufacture of board coffins; pooling of equipment and personnel of private mortuaries in emergencies; identification procedures; burial places for unclaimed and unidentified bodies; preparation of mortality lists; and arrangements with adjacent communities for mutual aid.

Morgue facilities should include a main morgue, usually the community's public morgue, and supplementary morgues as necessary to provide space for bodies in a ratio of 2 per 1000 population in target areas. Skating rinks, gymnasiums, auditoriums and similar buildings are suggested.

The staff of the Emergency Mortuary Service as set out in the bulletin includes a physician to confirm deaths. Other members of the staff are the director, recorder, property officer, identification officer, coroner's or medical examiner's representative, morgue attendants, clerical assistants and receptionists.

It is recommended that the identification tags used in the field casualty service for wounded be attached also to the dead in the field. Whenever possible a physician should examine bodies before they are removed to a morgue, so that if there is doubt of death in any case, the body may be taken to a casualty station or hospital for observation.

The bulletin outlines procedures for the reception of bodies at the morgue, the handling of personal property, the storage of bodies, identification and the release and disposal of bodies. Special measures for the handling of gas-contaminated bodies are described.

Federal funds are available under certain conditions to pay funeral and cemetery expenses. Mass disposal of bodies, either by burial in a common grave or by cremation, should be used only in the event of extremely large numbers of casualties which overwhelm regular and emergency mortuary facilities, and create a public-health menace.

The bulletin deals briefly with the reporting of casualties and recommends that information be released through the Casualty Information Service. Plans are also presented for the safeguarding of valuables and for the completion and storage of the morgue records.

MISCELLANY

DR. WILINSKY'S SIXTIETH BIRTHDAY

On Sunday, December 20, approximately three hundred and fifty persons assembled at the Nurses' Home of the Beth Israel Hospital to honor the sixtieth birthday of Dr. Charles F. Wilinsky. The speakers included Judge and Mrs. Abraham E. Pinanski, Judge A. K. Cohen, Mr. James Hamilton, president of the American Hospital Association, and Dr. Samuel A. Robins. Dr. Wilinsky was presented with a handsomely bound volume containing several hundred congratulatory letters from his friends in various parts of the country, several checks of appreciable amounts for the use of the Beth Israel Hospital and a portrait painted by Jacob Binder.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1942

DISEASES	OCTOBER 1942	OCTOBER 1941	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	7	46	19
Chicken pox	291	571	415
Diphtheria	13	8	15
Dog bite	842	857	806
Dysentery, bacillary	315	43	50
German measles	58	35	27
Gonorrhea	384	351	412
Measles	541	373	321
Meningitis, meningococcal	12	8	6
Meningitis, other forms	3	3	–†
Mumps	401	335	197
Paratyphoid infection	13	6	3
Pneumonia, lobar	242	192	222
Scarlet fever	622	466	312
Syphilis	610	450	426
Tuberculosis, pulmonary	265	289	245
Tuberculosis, other forms	13	29	31
Typhoid fever	7	11	7
Undulant fever	6	6	4
Whooping cough	732	555	468

*Based on figures for preceding five years.
†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Braintree, 1; Easton, 1; Fitchburg, 1; Fort Devens, 1; Salem, 1; Wareham, 1; Weymouth, 1; total, 7.

Diphtheria was reported from: Billerica, 1; Blackstone, 1; Boston, 2; Fall River, 4; Lowell, 2; Springfield, 1; Taunton, 1; West Brookfield, 1; total, 13.

Dysentery, bacillary, was reported from: Lynn, 3; Quincy, 1; Salem, 1; Wrentham (State School), 309; total, 314.

Encephalitis, infectious, was reported from: Everett, 1; Somerville, 1; total, 2.

Meningitis, meningococcal, was reported from: Boston, 2; Cambridge, 1; Camp Edwards, 2; Dracut, 1; Everett, 1;

Fall River, 1; Fitchburg, 1; Lowell, 1; Revere, 1; Woburn, 1; total, 12.

Meningitis, other forms, was reported from: Athol, 1; Boston, 1; Holyoke, 1; total, 3.

Paratyphoid infection was reported from: Boston, 2; Malden, 1; Norwood, 1; Quincy, 2; Somerville, 2; Southbridge, 1; West Boylston, 4; total, 13.

Septic sore throat was reported from: Boston, 6; Brockton, 1; Cambridge, 2; Winchester, 2; total, 11.

Trichinosis was reported from: New Bedford, 1; total, 1.

Typhoid fever was reported from: Becket, 5; Boston, 1; Milton, 1; total, 7.

Undulant fever was reported from: Danvers, 1; Gloucester, 1; Lexington, 1; Medford, 1; North Adams, 1; Whately, 1; total, 6.

Communicable diseases in general showed the usual seasonal increase.

Record-high figures were attained by mumps for the fourteenth time during the past sixteen months.

Whooping cough, German measles, paratyphoid infection, syphilis and bacillary dysentery were all reported at record-high figures. An outbreak in an institution is responsible for the high figures for bacillary dysentery.

Diseases reported at figures above their respective five-year averages were measles, meningococcal meningitis, lobar pneumonia, scarlet fever, dog bite, pulmonary tuberculosis and undulant fever.

The figure for typhoid fever was equal to the five-year average of the disease.

Reported at figures below their respective five-year averages were anterior poliomyelitis, chicken pox, diphtheria and gonorrhea.

Tuberculosis, other forms, was reported at a record low incidence.

Animal rabies was again reported from the focus previously mentioned in Norfolk County.

ARMY–NAVY "E" AWARD TO WINTHROP CHEMICAL COMPANY

On December 17, the Winthrop Chemical Company was presented the Army–Navy "E" award for its production of drugs essential to the war effort. The ceremonies were held in the morning at the plant in Rensselaer, New York, and in the evening at the Hotel New Yorker, New York City, for the employees in that city. Dr. Morris Fishbein was the principal speaker at both occasions, and Brigadier General Charles C. Hillman and Rear Admiral Charles S. Stephenson made the award. Of the more than a hundred drugs being furnished by the Winthrop Chemical Company to the armed forces of the United Nations, the most important are Atabrine, Plasmochin, Naphuride, Avertin and the various sulfonamides.

NOTE

General Frederick F. Russell, professor of preventive medicine and epidemiology, emeritus, at Harvard Medical School, was recently awarded one of three William Crawford Gorgas medals by the Association of Military Surgeons of the United States. These medals and the attached honorariums have been made possible by a grant from John Wyeth and Brother, Incorporated, of Philadelphia, and the award to General Russell was based on his pioneer work in immunization against typhoid fever. The other recipients were Rear Admiral Edward R. Stitt and Brigadier General Jefferson R. Kean.

BOOK REVIEWS

Gynecology and Female Endocrinology. By Emil Novak, M.D., D.Sc. (hon., Dublin). 4°, cloth, 605 pp., with 425 illustrations. Boston: Little, Brown and Company, 1941. $10.00.

The difference between this and earlier work on gynecology is clearly seen in the section on menstruation. It was only a few years ago that such a chapter was devoted to the anatomic description of what happened locally in the uterine wall. The present work tells a sequential story, which embodies endocrinology, physiology and anatomy, and the reader appreciates that he is beginning to get a view of what makes the wheels turn.

It is through the newer knowledge of endocrinology that a more rational approach can be made to both functional and organic disorders of the female generative tract. Dysmenorrhea, menorrhagia, sterility and habitual abortion are a few of the conditions in which the experimentalist has been helpful. In addition to presenting these innovations, the author also questions some of the latest methods as experimental. For example, he states that the value of pregnant-mare serum in producing ovulation in women is still open to question. Busy clinicians require a sane evaluation such as this to overcome the obvious high-pressure methods of the commercial houses to push their products.

Because of the many new things in this book, one is likely to overlook the very excellent discussion on pathology, which is presented with the help of numerous illustrations, including some excellent colored plates.

Dr. Novak has written this book primarily for general practitioners and medical students, and operative technic has been deleted. The material has been judiciously selected, and the style of writing moves smoothly like a well-told story. The result is the finest work on gynecology in many years.

Solving School Health Problems: The Astoria demonstration study. Sponsored by the Department of Health and the Board of Education of New York City. By Dorothy B. Nyswander, Ph.D. 8°, cloth, 377 pp. New York: The Commonwealth Fund, 1942. $2.00.

This volume presents the details of a four-year study of school health services in New York City carried on during the period from 1936 to 1940. It outlines and discusses problems of administration, record forms, nurse's duties and opportunities, teacher's participatio.:, dental care and tests for visual and for auditory acuity, including the presentation of many forms and blanks that have been found useful.

The following quotation gives an idea of the progressive outlook of the study as a whole: "Statistics of defects found and defects corrected furnish no index of the health problems which any individual child may develop later; they offer no index that the larger objectives of school health service are being reached; they give no evidence of the quality of work performed; they are not adapted to a single good supervisory technique which seeks to find out how to give better continuing supervision to individual children." This better-continuing supervision is dealt with in a positive way wherever possible.

The book is one of quality, and worthy of the care with which it has been printed and bound. It should be of interest to all school health administrators — physicians, nurses, teachers and health officers.

NOTICES

ANNOUNCEMENT

DR. ARMAND M. GAMBOA announces the removal of his office from 496 Massachusetts Avenue to 483 Beacon Street, Boston.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	January 4	Paul W. Hugenberger
Haverhill	January 6	William T. Green
Lowell	January 8	Albert H. Brewster
Brockton	January 14	George W. Van Gorder
Worcester	January 15	John W. O'Meara
Pittsfield	January 18	Frank A. Slowick
Northampton	January 20	Garry deN. Hough, Jr.
Fall River	January 25	Eugene A. McCarthy
Hyannis	January 26	Paul L. Norton

GREATER BOSTON MEDICAL SOCIETY

The next meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital, 330 Brookline Avenue, Boston, on Tuesday, January 5, at 8:30 p.m.

Dr. Maxwell Finland will speak on the subject, "Current Problems in Acute Respiratory Infections." Discussion by Dr. Chester F. Keefer, Dr. Charles A. Janeway and Dr. J. E. F. Riseman will follow.

Physicians are cordially invited to attend.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, January 7, in the classroom of the Nurses' Residence at 6:45 p.m. There will be a case presentation, "A Question of Diabetes Insipidus," and the following motion pictures will be shown: "Otitis Media in Pediatrics" and "Otoscopy in the Inflammations." Dr. Margaret Noyes Kleinert will be chairman.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, January 6 — The Hemolytic Syndromes: A five-year progress report. Dr. William Dameshek.

Friday, January 8 — Some Interesting Cardiac Problems. Dr. Frank T. Fulton.

Wednesday, January 13 — Angina Pectoris (with motion picture). Dr. J. E. F. Riseman.

Friday, January 15 — Title to be announced. Dr. William Malamud.

Wednesday, January 20 — A Renal Complication of Sulfadiazine. Dr. Francis McDonald. Discussion by Dr. Edwin L. Prien.

Friday, January 22 — Clinicopathological conference. Dr. Henry R. Viets and Dr. H. E. MacMahon.

Wednesday, January 27 — Boeck's Sarcoid. Dr. O. J. Bateman, Jr.

Friday, January 29 — The Face as an Index to Emotional Disequilibrium. Dr. Benjamin Spector.

On Tuesday and Thursday mornings, from 9 to 10 o'clock, Dr. S. J. Thannhauser will give medical clinics on hospital cases.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH

The fifth Annual Congress on Industrial Health, sponsored by the Council on Industrial Health of the American Medical Association, will be held at the Palmer House, Chicago, on January 11 to 13. The complete program appears in the December 5 issue of the *Journal of the American Medical Association*. To those who are interested in the problems of industrial health — and, at the moment, this should include practically everyone who is engaged in any phase of medical acitivity — the meeting promises to provide a wealth of valuable and up-to-date information.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, JANUARY 3

MONDAY, JANUARY 4

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, JANUARY 5

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

*8:30 p.m. Current Problems in Acute Respiratory Infections. Dr. Maxwell Finland. Greater Boston Medical Society. Auditorium, Beth Israel Hospital.

WEDNESDAY, JANUARY 6

*9:00–10:00 a.m. The Hemolytic Syndromes: A five-year progress report. Dr. William Dameshek. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

THURSDAY, JANUARY 7

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*4:00–5:00 p.m. Parenteral Nutrition. Dr. Charles C. Lund and Dr. John McKibben. Peter Bent Brigham Hospital amphitheater.

6:45 p.m. New England Hospital for Women and Children. Monthly clinical conference and meeting of staff.

FRIDAY, JANUARY 8

*9:00–10:00 a.m. Some Interesting Cardiac Problems. Dr. Frank T. Fulton. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, JANUARY 9

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

JANUARY 6–29. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Notice above.

JANUARY 11–13. Annual Congress on Industrial Health of the American Medical Association. Notice above.

FEBRUARY 13. American Board of Obstetrics and Gynecology. Page 690, issue of October 29.

(Notices continued on page ix)

63rd Year

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MAY 6. New Bedford.

ESSEX NORTH

JANUARY 6.
MAY 5.

ESSEX SOUTH

JANUARY 6. Danvers State Hospital.
FEBRUARY 3. Lynn Hospital.
MARCH 3. Essex Sanatorium.
APRIL 7. Addison Gilbert Hospital, Gloucester.
MAY 5. Salem Country Club.

FRANKLIN

JANUARY 12.
MARCH 9.
MAY 11. Annual meeting.

All meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

JANUARY 6.
MARCH 3.
MAY 5.

MIDDLESEX EAST

JANUARY 27.
MARCH 17.
MAY 5.

All meetings are held at the Bear Hill Golf Club, Stoneham, at 12:15 p.m., except that of May 5, which will be held at 6:30 p.m.

MIDDLESEX NORTH

JANUARY 27.
APRIL 28.
JULY 28.

PLYMOUTH

JANUARY 21. Brockton Hospital.
FEBRUARY 18. Jordan Hospital, Plymouth.
MARCH 18. Goddard Hospital.
APRIL 15. Bridgewater State Farm.
MAY 20. Lakeville.

WORCESTER

JANUARY 13. St. Vincent Hospital, Worcester.
FEBRUARY 10. Worcester State Hospital, Worcester.
MARCH 10. Memorial Hospital, Worcester.
APRIL 14. Hahnemann Hospital, Worcester.
MAY 12. Annual meeting.

WORCESTER NORTH

JANUARY 27.
APRIL 28.
JULY 28.

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MASSACHUSETTS MEDICAL SERVICE SECTION

VOLUME 227 JULY 30, 1942 NUMBER Part Two

YALE ... AUG ... LIBR

DOCTORS LAUNCH MEDICAL SERVICE

Blue Shield Adopted as Emblem

Making their contribution to the health of the people of the Commonwealth, Massachusetts physicians last week formally launched their voluntary system for prepaid budgeting which will equalize the distribution of medical care for the low-income groups.

With the full sponsorship of the Massachusetts Medical Society, the newly formed MASSACHUSETTS MEDICAL SERVICE adopted the Blue Shield as its emblem, determined subscribers' rates and physicians' compensation, and joined forces with the Blue Cross non-profit plan for hospital care. It thus set in motion a non-profit service based on the experience of other sections of the country and organized to meet a growing social problem.

Enrollment of doctors will begin August fourth, with the purpose of making the Blue Shield available to an eager public shortly after Labor Day.

Announcement was made jointly by Dr. James C. McCann, Blue Shield president, and George Putnam, Blue Cross president, that the new service will be administered by the Blue Cross. Operating as completely independent corporations, they will have the same executive director, R. F. Cahalane, under whose leadership the Blue Cross has rolled up a total of more than 400,000 subscribers. The Blue Cross field staff will also represent the Blue Shield with the first objective that of gaining 100 per cent physician-participation.

Subscribers' rates for the initial contract, which covers hospital surgery, obstetrics and diagnostic X-ray, are being determined by the directors and are subject to the approval of the State Commissioner of Insurance. They will be well within the budget of the low-income group.

On this basis, physicians' services will be provided regardless of cost to members of employed groups whose individual income is $2,000 or less and whose family income is $2500 or less. For people whose incomes are above this level, the plan offers protection in accordance with an established fee schedule.

LAUNCHING BLUE SHIELD
Shown l. to r. are Dr. J. Harper Blaisdell, Boston; Oliver G. Pratt, Salem; R. F. Cahalane, executive director, Blue Cross; Dr. James C. McCann, Worcester, Blue Shield president; and P. A. O'Connell, Boston.

The campaign for doctor enrollment will start with the mailing of a detailed Blue Shield brochure to every licensed physician in the state, enclosing fee schedules and contracts. The campaign goal is 100 per cent physician - participation, even though some medical men will not be actively involved in the initial step of what will become a complete medical service.

Blue Shield headquarters have been opened at 230 Congress Street, Boston.

Reprint, July 2 Issue
THE NEW ENGLAND
JOURNAL OF MEDICINE

McCann Named President by Board

Dr. James C. McCann of Worcester was elected president of the MASSACHUSETTS MEDICAL SERVICE at the first meeting of the Board of Directors held at the Harvard Club in Boston on June twenty-third.

Serving as vice-president is Philip M. Morgan, treasurer of the Morgan Construction Company of Worcester. Edmund L. Twomey, attorney, of Newton was elected treasurer. The Board Meeting was the first step in a comprehensive program which will attemp... state-wide system... geting of medical ... to the public short... Day.

Pointing out th... profession is u... radical departure ... vious mode of ... McCann stated ... cians are ready ... obligations in ... the high cost of ... according to the A... ciples of democrac... time maintaining ... of private initiat... practice.

The launching ... SACHUSETTS MED... should lead to a ... betterment of civ... Dr. McCann said ... maintenance of he... trial groups, and ... assuring the famil... in the armed for... medical-care bur... lightened.

Simultaneously, ... announced that t... setts Medical Soci... lished capital fund ... start the corporati... and that Boston ... had been opened a... Street. The corpo... was granted by th... missioner of Insu... twenty-seventh.

OUTLINES SUMME...

The first step in ... program, accord... McCann, is enrol... participating ph... said that an att... made for 100 per... ment among the ... maining in civiliar... that he anticipate ... cians going into th... pledge their suppo...

The plan, as re... June 18 issue of ... will provide budg... of the full medica... pital surgery, ob...

X-ray for families with incomes not exceeding $2500 yearly and for families with larger incomes on a cash indemnity basis. Later it is proposed to extend the coverage and the benefits.

Dr. McCann has been a surgeon in Worcester since 1929. Native of Bangor, Maine, he was graduated magna cum laude from Georgetown University in 1920 and from the Harvard Medical School in 1924.

He received his Ph.D. in surgery at the Mayo Clinic of the University of Minnesota in 1929, and held a lieutenancy in the army in 1918-19. He is married and the father of six children.

Morgan, vice-president of MEDICAL SERVICE, is a YD veteran of the first world war who is treasurer of the Morgan Construction Company of Worcester, director of the Mechanics National Bank of that city and of the State Mutual Life Assurance Company, trustee of Springfield College and Governor Dummer Academy, a director of the Massachusetts Safety Council and member of the executive committee of the National Safety Council.

Twomey, treasurer-elect, is a graduate of Holy Cross College and, in 1926, of Harvard Law School. He has practiced for many years with the Boston law firm of Palmer, Dodge, Barstow, Wilkins & Davis. He is married, father of one son, and lives at 22 Islington Road, Auburndale.

PHYSICIANS TO SERVE ON BOARD

Members of the medical profession are represented equally with laymen and subscriber representatives on the Board of Directors of the Massachusetts Medical Service.

In addition to Dr. McCann, who is serving as president, the physicians are Dr. J. Harper Blaisdell, Dr. Frank R. Ober, and Dr. Samuel A. Robins of Boston; and Dr. Charles E. Mongan of Somerville. They have been appointed to the central professional committee of the new non-profit corporation.

Born in Providence, Dr. Blaisdell was graduated from Dartmouth College in 1907 and from the Harvard Medical School in 1911 and has practiced in Boston since 1914 as a dermatologist. Assistant dermatologist at the Massachusetts General Hospital for twelve years, he is now consulting dermatologist for the Winchester, Melrose, Malden, Haverhill, and Exeter, New Hampshire hospitals. He is a director of the Blue Cross and a member of the Council and the public relations committee of the Massachusetts Medical Society.

Retiring president of the Massachusetts Medical Society, Dr. Ober was born in Mt. Desert, Maine, and was graduated from Tufts Medical School in 1905. He came to Boston in 1914 as house surgeon at the Boston Children's Hospital. Since 1937, he has been the John B. and Buckminster Brown Clinical professor of orthopedic surgery. He is assistant dean of graduate courses at the Harvard Medical School and professor of orthopedic surgery at the University of Vermont Medical School. He is also surgeon in chief of the New England Peabody Home for Crippled Children and orthopedic surgeon at Peter Bent Brigham Hospital.

He was a major in the Medical Corps, U.S.A., in the first world war and has been coeditor of a number of medical volumes.

Dr. Robins was graduated from the Tufts College Medical School in 1914 and did postgraduate work at the Tewksbury State Hospital and Boston City Hospital. Past president of the Greater Boston Medical Society, he is chief of the X-ray laboratories at the Beth Israel Hospital and was for fifteen years visiting roentgenologist of the Evangeline Booth and Boston Lying-In hospitals. He is consulting roentgenologist of the Norwood Hospital and Pratt Diagnostic Clinic.

Clinical professor of radiology at Tufts College Medical School and instructor in radiology at Harvard Medical School, he is the author of numerous articles.

A member of the House of Delegates of the American Medical Association since 1921, Dr. Mongan received degrees of A.B. and A.M. from Boston College and was graduated from the Harvard Medical School in 1892. He did post-graduate work at the Rotunda Hospital, Dublin, and studied at Guys Hospital and the Brampton Hospital for Tubercular patients in London.

Returning to Somerville as a general practitioner, Dr. Mongan has been a member of the senior staff of the Somerville Hospital since 1895, and is also a member of the staff of the Holy Ghost Hospital in Cambridge. He was the first president of the New England Obstetrical and Gynaecological Society and is a former president of the Massachusetts Medical Society. Recently he was appointed by the Mayor of Somerville as chairman of the advisory committee studying matters concerning public welfare.

Lay directors of the corporation are: Thomas G. Brown, vice president of the New England Trust Company, Boston; Philip Morgan, bank trustee and Treasurer of the Morgan Construction Company, Worcester; P. A. O'Connell, civic leader and president of E. T. Slattery Company, Boston; Oliver G. Pratt, bank trustee and Director of the Salem Hospital, Salem; and James Y. Scott, president of the Springfield Community Chest and president of the Van Norman Machine Tool Company, Springfield.

Representatives of the subscribers are: Daniel Boyle, Associate Commissioner of the State Department of Labor and Industries; J. H. Humphrey, Personnel Manager of the Dennison Manufacturing Company, Framingham; Ernest A. Johnson, Secretary-Treasurer of the Boston Building Trades Council, A. F. of L.; and trustee of the Boston Elevated Railway Company, Boston; Harold B. Leland, manager of Industrial Relations for the Hood Rubber Company, Watertown; and Roswell F. Phelps, Director of Statistics in the State Department of Labor and Industries.

Reprint, July 9 Issue
THE NEW ENGLAND JOURNAL OF MEDICINE

Wide Interest in New Plan

All licensed physicians in Massachusetts may participate in the Massachusetts Medical Service, according to Dr. James C. McCann, Worcester surgeon and newly elected president.

Since the public announcement of the launching of the new non-profit system for prepaid budgeting of medical care, headquarters at 230 Congress Street have been flooded with inquiries from physicians and laymen throughout the state.

"Chief query from the public," McCann states, "is when the service will be available. The speed with which doctors participate is the only answer, although early September is our goal. While the first contract is limited to surgery, obstetrics and diagnostic Xray, all physicians are urged to pledge their support even if they are not involved in the first contract."

Because physicians are asking for more detailed information about the new non-profit corporation, a series of articles has been prepared by the members of the plan's central professional committee. The first of these, dealing with the corporate structure of the organization, is published below. In the following weeks, the *Journal* will publish articles dealing with the service contracts, compensation for professional service, the doctor's relation to the service corporation, the relation of the MASSACHUSETTS MEDICAL SERVICE to the hospitals and the enrollment regulations of the Medical Service plan.

The Corporate Structure

JAMES C. McCANN, M. D.
President

Voluntarily, the medical profession is altering its economic relations with the public through the establishment of the MASSACHUSETTS MEDICAL SERVICE which is set up as a non-profit corporation. Complete legal protection for the new endeavor is provided by the corporate structure.

Since the doctors are placing control of many aspects of medical practice in the hands of the corporation, they may rightfully ask, "How does the corporation function?" It will function as does any business corporation. Members of the executive committee of the Massachusetts Medical Society constitute the voting members of the corporation and take the place of the stockholders.

Voting members elect the directors who, in turn, are the corporation's managers. The voting members can remove the directors from office if there is due cause. The only other restrictions on the directors' powers are those specified in the by-laws, those arising from the state insurance commissioner's interpretation of the enabling act and the by-laws, and by those arising out of recourse by any party to the courts.

SECURITY OF PHYSICIANS

It is vital that medical standards as related to the welfare and the rights of the doctors be protected when they become involved with the legal complexities of a corporation, and that there be professional supervision of the purely medical aspects of the new plan. This supervision is guaranteed by the fact that the voting members are, themselves, physicians representing the profession of the entire state.

DIRECTORS CAREFULLY CHOSEN

As described in the June eighteenth and July second issues of the Journal, the directorate of the Massachusetts Medical Service numbers fifteen members, representing equally the physicians who have direct contact with the medical profession through the local professional service committees in the districts; eminent laymen whose practical experience is of great value; and outstanding representatives of the subscriber groups.

LIAISON WITH THE PROFESSION

There are vital medical matters which might possibly be mishandled by such a composite corporation were it not for the organization and functioning of the board which is broken into committees assigned to specific tasks. The executive committee takes responsibility between the meetings of the entire directorate. The financial committee guards the funds and investments. The actuarial research committee compiles data which protects physicians through a sound actuarial procedure. The interlocking services committee supervises the relationship of the two independent but jointly functioning corporations—MASSACHUSETTS MEDICAL SERVICE

and the Blue Cross. The central professional service committee has power to initiate action for the board of directors on all vital medical matters, submitting to the board complete medical data as basis for any action by the directors. In effect, this last committee serves as a medical advisory committee to the directorate. Furthermore, any anticipated action by the central professional service committee will be reported thirty days before action is taken to the voting members, who can send resolutions and recommendations to the directors.

This assures full knowledge to the representatives of the profession of anticipated action by the directors on medical matters. The knowledge will also be available to the Council, whose resolutions or recommendations to the voting members would carry impressive weight.

INDEBTEDNESS TO LAYMEN

The medical profession of Massachusetts is privileged to have serving on the directorate some of the most eminent leaders of the state. These men are serving without compensation because of a sense of responsibility to the public and have accepted a trusteeship which will require much of their time and expert judgment. Remembering that the corporation is not an insurance company but strictly their own corporation formed by them to solve current problems in medical care, the physicians are greatly indebted to these civic minded lay-directors.

OPPORTUNITY FOR NEW PLAN

The MASSACHUSETTS MEDICAL SERVICE, established after long years of study and based on the experience of other medical care plans throughout the country, has the opportunity of meeting changing conditions and, at the same time, preserving basic freedoms. Physicians and patients can retain the freedom of choice and freedom to serve; the freedom as to form of treatment and the freedom with reference to financial compensation.

Through this new corporation, the medical profession of Massachusetts can meet satisfactorily the challenge of the times.

Reprint, July 16 Issue
THE NEW ENGLAND JOURNAL OF MEDICINE

Income Limits Determined for Subscribers

In an effort to create for the low-income employee groups a larger measure of protection than a cash-indemnity contract provides, the MASSACHUSETTS MEDICAL SERVICE faces the unwelcome necessity of determining income limits below which medical service contracts will be sold.

Medical-service contracts refer, of course, to the services that will be provided by participating physicians for surgery, obstetrics and diagnostic X-ray studies. The term is used in contrast to the cash-indemnity, or limited, contracts that will be available to individuals in any income bracket above the specified limits. The Massachusetts doctors are initiating their program by offering this medical-service contract only to members of employee groups whose individual income is $2000 or less or whose family income is $2500 or less. That such an arbitrary income limit is fair to both the physicians and the subscribers has been determined after serious study of medical-service programs throughout the country.

The states of California, Oregon, Washington, Michigan, North Carolina, and Pennsylvania, the counties surrounding Buffalo and Utica, New York, and the city of Dallas, Texas have plans well under way. Within recent months, New Jersey and Colorado physicians have established statewide plans. In all of these states the highest level to which the medical-service contract is available, ranges from $2000 to $3000.

Decisions in these pioneer states were based on surveys of income levels, on the requirements of state insurance departments, and on the need for a sufficiently broad base to render enough individuals eligible so as to meet the percentage requirements for group enrollment.

In California, physicians set the upper level of eligibility at $3000, the base figure in a comprehensive health-insurance bill which was nearly passed. Because the state insurance department would not accept lower levels, Buffalo set the limits at $1800 for the individual, $2500 for man and wife, and $3000 for the family. Utica has no limit on eligibility. New Jersey established $1600 as the level for the family, found it too low, and altered it to $2500 for the family on the basis of government legislation proposed for the low-income group. Michigan established the limit at $2000 for the individual and $2500 for the family.

BASIC FIGURES RESULT OF STUDY

In addition to the study of the plans operating in other states, the Massachusetts Medical Society has arrived at its $2500 base figure through a study of income groups in Massachusetts. The most normal of recent years was the year 1939-40, inasmuch as it was free from the abnormal influences of depression or boom. The study revealed that an individual income level of $2000 accounted for 83.4 per cent of the wage earners and that a $2500 family income embraced 91.4 per cent. In the present period of increasing wages, these percentages may be modified. With the increased cost of living, however, individuals within these fixed limits are even more in need of a medical-service program.

Employees whose individual or family incomes place them above the medical-service contract may be enrolled with their group on a cash indemnity basis. They will receive cash payments for medical services in the amounts specified in their contracts. Since this cash-indemnity subscriber may then be charged by the physicians the difference between the latter's fee and the amount guaranteed by the contract, there is virtually no alteration in the present financial arrangement between the private patient and his physician, except that the doctor is assured more prompt payment and the subscriber is enabled to pay his bill more easily.

Summarizing, then, the physicians of the state through the MASSACHUSETTS MEDICAL SERVICE are offering medical-service contracts, which comprise surgery, obstetrics, and diagnostic X-ray services to groups of employees whose individual incomes are $2000 or less and whose family incomes is $2500 or less; and a cash-indemnity contracts for employees whose incomes are above these figures.

Reprint, July 23 Issue
THE NEW ENGLAND JOURNAL OF MEDICINE

First Contract Initial Step in Complete Service

The public is not yet willing to buy complete medical service contracts, according to the studies made by the Massachusetts Medical Society of the medical plans in operation in other states.

Therefore, the MASSACHUSETTS MEDICAL SERVICE is initiating its program with a partial coverage contract which includes hospital surgery, diagnostic X-ray and obstetrics.

This first contract is the initial step in evolving a complete medical care service. Present plans indicate that the second contract will cover all hospitalized illnesses and that the third contract will cover hospital, office and home care insofar as experience proves it advisable.

This gradual approach parallels the method used in developing the Blue Cross non-profit plan for hospital care and is based on the need for educating the public gradually to the need for increasing expenditure in order to obtain more complete services. The Blue Cross contract was sold first to the individual subscriber on the basis of three cents per day; next, the subscriber was willing to spend more in order to protect himself and his wife; and finally, the subscriber learned the value of buying a more expensive contract which would protect his family, which includes all unmarried children under nineteen years of age.

OTHER STATES POINT THE WAY

The wisdom of a gradual development of the Massachusetts plan is borne out by the experience of medical service plans in other states, where complete coverage has met with poor public response.

In Michigan, 187,000 surgical-obstetrical contracts were sold as against only 5816 complete medical coverage contracts. In one year alone, Michigan lost $75,000 on complete coverage contracts, of which $10,000 was lost on a single employee group. California has sold only 30,000 complete coverage contracts in six years and only 10,000 have been sold in New York.

PREMATURE CONTRACTS UNSATISFACTORY

The premature sale of complete coverage contracts to a public uneducated to them brings disastrous results in many instances. In some states, compensation to family physicians dropped to from twenty to sixty cents on the dollar. In other states, the medical service corporation went into debt in order to maintain payments to physicians.

Buffalo, California and Michigan are selling no more complete coverage contracts and all of the states which began with complete coverage contracts have been forced to revert to the issuance of the surgical-obstetrical contract.

"The surgical benefit contract is more or less predictable from an actuarial basis," writes Philo Nelson, general manager of the California plan, "and is the soundest to begin with."

John Mannix, executive director of the Michigan Hospital Service, who is closely affiliated with the Michigan Medical Service, states:

"From the experience of Michigan, partial coverage is the only approach that is reasonable."

The wisdom of the partial coverage contract is further confirmed in a preliminary re-

(Continued on page 4, col. 4)

Blue Shield Joins Forces with Blue Cross

To Function Together

The Council of the Massachusetts Medical Society accepted the following recommendation at its meeting on February 4, 1942:

"That permission be granted MASSACHUSETTS MEDICAL SERVICE corporation to coordinate its activities with the Blue Cross relative to (1) the presentation of joint contracts to subscribers and (2) administrative function and expense. This shall be done with each group retaining (1) its distinct corporate identity and (2) the right to issue separate contracts, the relation of the two corporations to be determined on a contract basis."

By this action the Council accepted the logic of events in other states. The medical societies of California, Michigan, Buffalo, Utica, New Jersey and elsewhere, have proceeded in this manner with joint activities on a contract basis with the local non-profit Hospital Service corporations. The objectives of the two corporations are similar; the subscribers to both plans are virtually the same; the functions of the office and sales force are essentially identical in character. To proceed independently of the non-profit hospital service corporation which has preceded the medical service corporation in the field, would entail unnecessary duplication of work force and expense. It would be confusing to the public. The medical society would have to evolve separately and painfully all the techniques which have been perfected through the years by the Blue Cross. There is only one major requirement involved in this close relationship—each corporation must retain its distinct corporate identity and powers. This separate identity is safeguarded by a renewal contract made under the supervision of the Commissioner of Insurance.

SAVES COST

The value of such a liaison is apparent. Of major importance, considering the non-profit character of both corporations, is the considerable reduction in operating costs which will accrue to both. Moreover, when the established expense is diluted by an expanding volume of business, there remains a larger quantity of service available for each dollar the subscriber pays. It has been variously estimated that the overhead expense for the Blue Shield will be reduced from a probable 15 to 17 per cent as an independently functioning corporation to 10 or 11 per cent on the basis of joint administration with Blue Cross. This means significant savings to the subscriber, and greater protection of professional fees for the doctor. On one item of office expense alone ($1800 per month for International Business Machines) the saving is considerable. Duplication of the office force is avoided. For the Blue Shield to build up and train a sales force in the field would entail serious delay in effective operation and excess expenditure of needed funds.

The open entree which the sales staff of Blue Cross enjoy after several years' work in the field would be developed by the Blue Shield with difficulty. Busy personnel managers would be slow to accept the representatives of an entirely new and separate organization, even though they represented the profession of medicine. In contrast stands the assertion of one manager in answer to inquiries from Blue Cross as to whether he was interested in the medical society program. He said, "If the Blue Cross says it's all right, it's all right with me."

SINGLE PAYROLL DEDUCTION

There are cogent reasons from industry and trade as to why it is imperative that Blue Cross and the Blue Shield function in close harmony and cooperation. It is desirable that all group memberships be sold on the basis of payroll deduction of premiums. Responsible managers in industry request that there be but one payroll deduction for a joint contract. It might be impossible in the face of income tax, war bond and other deductions to procure an additional deduction for a medical service contract. Also the public looks upon hospital and medical expense as one single episode. When purchasing protection against these allied hazards, they seek a "single package," which provides for the total expense of hospital illness. If payroll deduction is not available, the subscribers find it confusing and bothersome to arrange for separate small monthly payments on two contracts.

The public attitude was forcibly presented by Louis H. Pink, Superintendent of Insurance in New York, recently, when he addressed the New York Academy of Medicine. He criticized the failure of the medical societies to cooperate with the Hospital Service plans; he suggested that the two services should be closely bound together. Organized medicine wants, he said, "strict separation of something which, it seems to me, is not easily or properly separable." With the promising background of mutual trust and understanding which exists between Blue Cross and the Blue Shield in Massachusetts, both corporations as well as the public should profit and benefit by this natural alliance.

INCREASES PUBLIC CONFIDENCE

The Blue Shield should not look lightly upon the benefits to be derived from this association. Blue Cross after five years of effort has enrolled more than 400,000 subscribers in Massachusetts and enjoys great public confidence and support. Blue Cross groups have been formed in more than 5000 industrial and business organizations in Massachusetts. It would be shortsighted for the Blue Shield to overlook the public confidence which will meet our offering when presented jointly with the widely accepted Blue Cross service.

On the basis of the contract drawn between the two corporations, the employees of the Blue Cross, by proper allocation of funds, now become the salaried agents of the Blue Shield. As such, they will sell the medical service contracts to the public. Also as agents of the Blue Shield they will make personal contact with the individual physicians in the state seeking their cooperation and support, and seeking to answer questions which will inevitably arise. On August 4, these men will begin their field work among the doctors in the state, urging their enrollment as participating physicians. The enrollment of an adequate proportion of the profession is essential before sale of memberships to the public can begin. As these men visit your office, please recognize that, even though they continue as Blue Cross employees, they are also bona fide salaried representatives of the doctors' corporation, the Blue Shield.

It is hoped that these men will be cordially received as the accredited representatives of the Blue Shield plan, sponsored by the physicians of the Massachusetts Medical Society.

First Contract Initial Step in Complete Service

(Continued from page 3, col.

port made by the New York State Superintendent of Insurance, who states:

"A greater appeal seems to exist for surgical benefits than for general medical coverage. This is due perhaps to the possibility of being confronted with much more substantial bills for surgical services than for general medical expense. It is understood that the plans contemplate experimenting to a greater extent in this field."

By enthusiastically and actively supporting the program of the MASSACHUSETTS MEDICAL SERVICE, physicians of the state may help to avert the appearance in Massachusetts of a bill similar to the following which will be supported next year in the New York Insurance Commission unless the New York medical profession takes active steps.

"A hospital corporation may by amendment of its charter acquire the power to supplement its contracts for hospital service by provision for the furnishing of indemnity against physicians' fees for surgical and obstetrical care rendered." (Hampton Bill, New York Senate No. 1273 Int. 1054.)

All communications relative to the Massachusetts Medical Service should be addressed to

MASSACHUSETTS MEDICAL SERVICE

230 Congress Street
Boston, Massachusetts
Telephone: Hubbard 8800

R. R. A

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MASSACHUSETTS MEDICAL SERVICE SECTION

Volume 227 SEPTEMBER 3, 1942 Number 10, Part Two

BLUE SHIELD PRESIDENT OUTLINES CAREFUL DEVELOPMENT

TRACES STEPS IN LAUNCHING PLAN

Urges Doctor Cooperation

by James C. McCann, M.D.
President

Massachusetts Medical Service stands on the eve of its launching. A high-pressured schedule has been met with an insignificant lag of a couple of weeks. The difficulties of interlocking the innumerable related aspects of documents to be presented to the public and to the doctors has rendered this slight delay unavoidable. However, the interest of good public and doctor relations for the corporation have rendered ill advised any effort to beat the time clock at the expense of accuracy and clarity.

Within the week, mailing of pertinent data to every individual physician in the state will have begun. Enclosed with this data will be a contract between the physician and the corporation. The purpose is that the doctor may completely inform himself on all important aspects of the program before he signs the contract. It is hoped that in view of the broad character of the present contract every physician will sign. Every physician who uses any hospital obstetrics, orthopedics, anaesthesia, surgery, medical consultation or assisting on surgical cases is essentially involved by the contract.

We should hope for and procure nearly 100 per cent participation by physicians in this first contract, as nearly all may have occasion to deal with subscribers from one or another angle in this first contract. Even though the call to participate may be limited, every physician should consider the wisdom of enrolling so as to present public evidence of an intact responsible profession giving full support to the program of medical care which it has initiated.

Several meetings of the Board of Directors, and special committees, and of representatives of Blue Shield and the State Insurance Group, have worked over repeatedly the many exact items which had to be prepared. Chief, of course, among them was the subscribers contract. This provides for surgical, obstetrical and orthopedic services for hospitalized patients. Anaesthesia and such endoscopic services as are related to the surgical experience are provided for. X-ray services to the extent of $15 (which accounts of 70 per cent of all X-ray required in Michigan) are provided for in the hospital and within the roentgenologists' office for a period of thirty days preceding the surgical experience. The balance of X-ray services is paid for by the patient. For the unlimited service group (low-income) restricted assistant and consultation services are arranged for on the basis of proportion of the total benefit allowed in the fee schedule for the particular service. Under the guidance and supervision of the Insurance department, the contract has been rewritten many times, until it seems finally to have achieved an accurate, satisfactory character from the view point of the subscriber, the doctor, and insurance authorities. It is thus evident that practically all groups in the profession may be called upon to render service under the terms of this initial presentation of Massachusetts Medical Service.

Of considerable importance were the other two contracts which had to be prepared. The first relates to the relationship between the Blue Shield and the Blue Cross. Under the direction of the Commissioner of Insurance, the business aspects and enrollment procedures of the Blue Shield will be carried out by the personnel of the Blue Cross. These groups will act as the accredited and paid agents of the Blue Shield. R. F. Cahalane, Executive Director of the Blue Cross, at present is

(Cont. on Page 3)

SIGNING UP AS BLUE SHIELD DOCTORS

Miss Betty Long, Blue Shield representative, shown with members of the Middlesex South Medical Society who signed up as participating physicians in the Blue Shield. L. to r. are Miss Long, Dr. James M. Baty, Belmont; Dr. Hollis L. Seavey, Cambridge; Dr. John J. Grinold, Belmont and Dr. William J. Moriarty, Belmont. (See story, page 2.)

SAMPLE CASE HISTORIES
EXPLAIN BLUE SHIELD METHODS

The public education department of the Blue Shield has prepared a series of sample case histories, illustrating the methods of Blue Shield procedure. The first of these appear below.

UNLIMITED SERVICE BENEFIT (SURGICAL) SAMPLE CASE NO. 1

Mrs. John X. is the wife of a factory worker and the mother of two children. Mr. X. is the only employed member of the family and his wages, during the past year, have totaled $1,900.

On October 1, Mr. X. joined the Blue Shield with a group of fellow employees, so that he would be financially able to meet any unforeseen doctors' bills for services covered by the medical plan.

On November 5, Mrs. X. consulted her family physician, who diagnosed her condition as an acute disturbance of the gall bladder. Her family physician referred her to a surgeon who, with the diagnosis confirmed by X-ray, recommended an immediate cholecystectomy. Arrangements were made for Mrs. X. to enter the hospital where the surgeon cared for his surgical cases on November 6. Operation was performed within a few days, with the anaesthesia given by a salaried nurse in the hospital and paid for by the Blue Cross. Two weeks later, Mrs. X. was discharged from the hospital.

The family physician, the surgeon and the roentgenologist who treated Mrs. X. were participating physicians in the Massachusetts Medical Service.

The surgeon and roentgenologist reported the case promptly to the Blue Shield on forms furnished for the purpose after completion of treatment. The surgeon received a payment of $125; and the roentgenologist $15.

EXPLANATION

Mrs. X.'s Blue Shield certificate entitled her to service without extra charges by virtue of the fact that her annual family income was within the $2,500 limit.

Payment to the physicians by the Blue Shield was made on the following basis:

Since the Blue Shield's established fee schedule calls for $125 payment for a cholecystectomy, the surgeon received this amount.

Total received by surgeon $125

The fee paid by Mrs. X. to the family physician for the initial visit outside the hospital was by private arrangement.

The roentgenologist received $15 for the gall bladder X-ray.

Total received by roentgenologist $15

Total Disbursement by the Blue Shield $140

UNLIMITED SERVICE BENEFIT (SURGERY) SAMPLE CASE NO. 2

Mr. Richard Y. is an unmarried executive earning $4,000 annually.

On October 7, Mr. Y. joined the Blue Shield with a group at his office with the privileges of a limited service contract.

On January 6, he entered the hospital for an acute appendectomy, upon recommendation of the surgeon whom he had consulted. On January 7, the operation was performed with no ensuing complications, and on January 17, Mr. Y. was discharged from the hospital.

Mr. Y.'s surgeon reported the case promptly to the Blue Shield after the operation. He received a payment from the Blue Shield of $75. In addition, he received a check for $25 from Mr. Y.

EXPLANATION

Mr. Y.'s Blue Shield certificate entitled him to a credit of $75. Payment of this sum was made to the surgeon by the Blue Shield. An additional $10 was paid by the Blue Shield to the physician administering the anaesthesia. Both these men were participating physicians in the Blue Shield.

Total Disbursement by the Blue Shield $75

Since Mr. Y.'s income was above the $2,000 individual income level for unlimited privileges and since the surgeon's regular charge for an appendectomy was $100, an arrangement had been made between Mr. Y. and his surgeon for the payment of the $25 balance of the bill.

UNLIMITED SERVICE BENEFIT (OBSTETRICS) SAMPLE CASE NO. 3

Mrs. George W. is the wife of a clerical worker in a small town office. The salary of Mr. W., the only employed member of the family, totaled $2,300 during the past year. Mr. W. joined the Blue Shield with his office group on October 1.

On the following August 1, Mrs. W. became pregnant and consulted her family physician. A participating physician in the Bue Shield, her doctor took full charge of Mrs. W's case, giving her adequate pre-natal care and arranging for her admittance to the hospital for delivery.

The delivery was normal, and after a hospital stay of two weeks, Mrs. W. returned to her home with her baby, continuing as a patient of her family physician for post-natal care.

The case was reported promptly to the Blue Shield on forms furnished for the purpose. The family physician received from the Blue Shield a payment of $40. He also received a payment from Mrs. W.

EXPLANATION

Mrs. W.'s Blue Shield certificate entitled her to delivery and care in the hospital without extra charges by virtue of the fact that her family income was within the $2,500 limit.

She was eligible for this service because she had been a Blue Shield member for more than the 9 months required by her membership certificate.

Payment to the physician was made on the following basis:

Since the Blue Shield's established fee schedule calls for a payment of $40 for delivery with complete care in the hospital, the physician received this amount.

Total Disbursement by the Blue Shield $40

In addition to the payment to him by the Blue Shield, Mrs. W.'s doctor received a payment from her for prenatal and post-natal care in the office. This fee was a private arrangement between Mrs. W. and her physician.

Middlesex South Physicians Sign Up

First district medical society to give its official endorsement to the Blue Shield is Middesex South, which held its adjourned annual meeting and mid-summer meeting on Wednesday, August 12, at the Oakley Country Club in Belmont.

Dr. Brainard F. Conley of Malden, who was instrumental in putting through the Enabling Act for the medical service plan, addressed his fellow members and pointed out to them the value of Massachusetts Medical Service, which is sponsored by the Massachusetts Medical Society.

"We are being given the opportunity," Dr. Conley said, "to render a real community service and at the same time to establish for ourselves the soundest kind of prepaid budgeting for medical care."

"Here is our chance," Dr. Conley continued, "to help solve one of today's most serious national problems — the distribution of private medical care in civilian communities. We know that this job must be done, and the Blue Shield is the doctors' own answer to a growing challenge on the home front."

Following Dr. Conley's address, Dr. Hilbert F. Day, president, declared a recess in order to give the members an opportunity to go on record as the first participating physicians in the Blue Shield.

Because the contracts were still being studied by the State Department of Insurance, Blue Shield representatives circulated the following agreement for signatures:

I hereby agree in principle to the Plan for Surgical and other services to be offered by Massachusetts Medical Service, and agree to become a Participating Physician upon receipt of the terms and conditions of participation, provided that the final draft of the various documents is not changed in principle.

....
Date **Signature**

A hundred per cent of the 117 members who attended the meeting signed the agreement, thus setting in motion what promises to be a successful state-wide enrollment of participating physicians in the Blue Shield.

Two hundred and fifty-four Councilors of the Massachusetts Medical Society have signed the agreement to become participating physicians in the Blue Shield, pointing the way for their fellow members who will be enrolled this month.

Urges Doctor Cooperation
(Cont. from Page 1)

acting also as the lay executive director for the Blue Shield. The future development of Blue Shield personnel must be deferred until such time as the complexity of the program make other services necessary, and corporation finances makes other salaries possible. The third important contract is that by which the physician signs with the Corporation as a participating physician.

The fee schedule is a matter of great importance to which much time and study has been devoted. It is essentially based upon a fusion of many established fee schedules and modified to fit the practices in Massachusetts. It is based on the New York Workmen's Compensation Schedule, the Baker Memorial schedule, the schedules in effect in the Northern New York plans and the Michigan Medical Service schedule. The latter schedule, the most important of the group, and quite parallel to the Baker Memorial schedule, was developed from a study of many of the fee tables developed in the country, and extensive surveys of charges in the State of Michigan which quite parallel that of Massachusetts. The schedule developed on this basis was presented to a large group empowered by the Council of the Massachusetts Medical Society to study and approve the schedule — the Executive Committee, the Public Relations Committee and specialists appointed to give a satisfactorily balanced group. From this group two smaller advisory committees were appointed to help expand and clarify the schedules for orthopedic and neuro-surgical services. Together with the accompanying rules and regulations, which relate mostly to the workings of the fee schedule, it is expected that the bulk of services provided for under the first contract may be automatically administered with a minimum of special adjustments required.

Attention should be called here to the splendid cooperation shown by the state department of Insurance. When doctors land in the morass of business or insurance, they would be guilty of the most naive errors were they not carefully guided by such experts as those who are in the Insurance department. They have given very generously of their time in clarifying contracts and giving advice for avoidance of pitfalls which might trap the unwary physicians. It is well for the profession to be informed of this invaluable and understanding service to our cause.

The major effort which must be carried out first by the Corporation is the enrollment of physicians. No offering of contracts to the public can be made until an adequate enrollment of participating physicians is secured so as to guarantee adequately available service for the subscribers. The enrollment for the most part must be based on a voluntary signing of contracts by the physicians of the state. To personally contact seven thousand physicians in a few weeks is obviously impossible. All physicians are asked to sign their contracts and return them early. A certificate suitable for framing and office display will be sent to each participating physician. It is particularly hoped that the men who are departing for service in the armed forces will sign the contract before they leave so that the public may be thoroughly impressed with the fact that this is truly the doctors' program. Already key groups have begun to sign as a group. The members of the Executive and Public Relations Committee who were present at the fee schedule meeting signed as a group. The Middlesex District Society at a mid-summer meeting signed up one hundred seventeen strong. This portends well for the necessary doctor interest to make the program a success. As a follow up to the contracts, the lay sales force of the Blue Shield will personally contact physicians who have delayed in mailing in their contracts, to clarify any problems in their minds, and to help forgetful ones to get their contracts into the mail.

Massachusetts physicians are particularly fortunate in having their program launched under such favorable auspices. There has been and is a basic unity of purpose in the entire profession of the state regarding this problem of medical care. We have been spared the difficult experience of other states which have guided us to a sound approach to the problem through partial coverage contracts which will gradually expand to complete coverage as the corporation is established on a sound financial, administrative, actuarial and professional base.

The profession has none too much time in which it can demonstrate its capacity as a fine profession to manage these difficult problems in medical economics and in the distribution of medical care. Time is fleeting and the pressure for bureaucratic medicine is growing apace. Can we achieve a demonstration of that professional unity, self discipline and capacity necessary to solve that aspect of the growing social problem confronting America, which is our present responsibility? The demonstration of it will come from every Massachusetts physician signing his contract to participate; by his giving whole-hearted support and cooperation to this Corporation of his own creation; and by exercising patience and forebearance in the early difficult days while his Corporation learns to walk. Later we shall run. Massachusetts Medical Service stands on the eve of its launching. Put your shoulder to the task and clear the ways! Sign your Contract!

FORTUNE SURVEYS PUBLIC OPINION ON SOCIALIZED MEDICINE

In its July issue, Fortune posed the following question in regard to socialized medicine:

"Do you think the Federal Government should or should not collect enough taxes after the war to provide medical care for everyone who needs it?"

The tabulation showed that 74.3% of the people thought that the government should; 21.0%, that it should not; and 4.7% said they did not know.

There was not a single dissenting majority in any income or occupational group or in any section of the country.

Reprint, August 30 issue
NEW ENGLAND JOURNAL OF MEDICINE

A CORRECTION

To the Editor: It has come to my attention that you have reprinted my article "Unsocialized Medicine," in a special supplement to your journal. I was pleased to have my dissenting remarks included among the newspaper pieces lauding the new prepayment plan of the Massachusetts Medical Society, and was impressed by the profession's tolerance of my somewhat sharp criticisms.

However, you erred in identifying me as "president of the White Cross," and I'd appreciate your correcting this so as not to expose the White Cross (which supported the Massachusetts Medical Society legislation) to professional criticism for my personal views.

Francis H. Russell, now with the State Department in Washington, is president. Edward A. Taft, vice-president and Boston lawyer, has been acting president during his absence. I functioned only as president of the unofficial but enthusiastic Association of White Cross Members.

Harold Putnam

The Boston Globe
Boston

* * *

The *Journal* acknowledges its error of referring to Mr. Putnam as president of the White Cross. Incidentally, it is pleased to learn that the views of Mr. Putnam are purely those of an individual and not those of an organization — either the White Cross or the Association of White Cross Members. Ed.

COMPULSORY INSURANCE DISCUSSED ON AIR

Coast-to-Coast Broadcast Heard by Millions

By Nathalie Harris Mann

Millions of Americans tuned in last Sunday night, August 30, from 8 to 8:45 p.m. to hear a lively discussion on the coast to coast network of the Mutual Broadcasting System of "Is Compulsory Health Insurance in the Public Interest?"

In Massachusetts alone, eight stations carried the program which brought forcefully to the attention of the people of the state the subject which is provoking increasing interest.

The Forum was moderated by its founder and chairman, Theodore Granik, attorney and editor. Participants were: affirmative: Dr. Ernst Boas, Chairman, New York Physicians Forum for Study of Medical Care and Assistant Clinical Professor of Medicine, Columbia University, and Dr. Miles Atkinson, Author of "Behind the Mask of Medicine"; negative: Dr. Morris Fishbein, Editor, Journal of the American Medical Association, and Dr. Edward H. Cary, Chairman of the Board of Trustees, National Physicians Committee for the Extension of Medical Services, and past President of the American Medical Association.

NO CREDIT TO DOCTORS

Commending health conditions and the low death rate in the United States, Dr. Boas asserted that representatives of organized medicine have given the American medical profession complete credit for this state of affairs and have claimed that it results from the present system of free enterprise. Actually, he stated, it is due simply to the better economic status of our population and pointed out that the poor sections in this country that are in the greatest need of medical care do not get it.

Since the health of its citizens and workers is the concern of the government, the government must necessarily take a hand, he said. Experience with Old Age Security and Workmen's Compensation Insurance has shown that to be effective, health and sickness insurance must also be compulsory for all persons of certain income levels. He said it would be pernicious to plan universal distribution of second-rate medical care, and the assurance of high quality is primarily a professional problem. He recommended that the physician through the medium of his organizations must be given free hand to develop the best techniques and that an insurance plan must be set up to provide group medicine centered about clinics and hospitals where all needed facilities are available, where the general practitioner makes his headquarters and where he has at hand all the specialized help he may need.

DR. CARY UNCONDITIONALLY OPPOSED

Dr. Cary expressed himself as unconditionally opposed to any form of compulsory health insurance in the United States. He stated that the lowest average level of medical service in this country is equal or superior to any service offered to the general public in any other nation in the world. The medical profession's determination to give this care to the people has not resulted from legislation, he said, but from a medical effort to stimulate public opinion. American medicine's superiority and unequalled effectiveness lies actually in its freedom from restraint and outside control, he said. Any form of compulsory insurance even under the most favorable circumstances introduces into the treatment of disease a third and disinterested party. Funds that should be spent for the sick are diverted to the vast number who must administer a new system. Standards necessarily become fixed and such a system would destroy the physician's incentive to greatest efficiency.

This would undoubtedly lower the quality of medical care, he said, and those who would suffer most would be not the doctors but the general public.

ATKINSON POINTS TO ENGLAND

The word "compulsory" was under scrutiny in Dr. Atkinson's presentation. Admitting that no one likes to be compelled, he stated that, nevertheless, compulsion was often necessary and cited taxes as working for the common good of the people. He suggested that the proposed name of Compulsory Health Insurance be changed to Community Health Insurance as a means of sugar-coating the pill. Stating that something must be done to help the little man, Dr. Atkinson asked his audience to consider the success of the National Health Plan in England. At the outset of the plan in 1911, he said, the British Medical Association, a body closely analogous to the American Medical Association fought it with the arguments now being produced in this country — bureaucracy, lowered standards of practice, loss of individual initiative. Today, he said, nobody in England would return to the old days or the old ways, and there is no doubt in the mind of the public and of the members of the British Medical Association that compulsion is in the best public interest.

NO BENEFIT TO WORKER, FISHBEIN SAYS

Compulson is not the American way and leads to a slavish not a democratic population, according to Dr. Fishbein.

Refuting his opponents' arguments, Fishbein stated that proof is available to show that compulsory health insurance increases rather than decreases the cost of medical distribution; that preventive medicine is not further advanced in countries utilizing the compulsory system than it is in the United States; that medical resources are frequently wasted in unnecessary and superficial treatment of minor diseases and that serious, catastrophic illnesses are neglected.

The average number of days lost through illness by the compulsory insured workers of Germany and England is twice as high as those lost by wage earners in this country. Furthermore, diagnosis and treatment tend to become mechanical and superficial. Most important, he said, once such a system is finally adopted, it becomes a bureaucratic department of the government with a vast number of employees directing their efforts toward making the bureaucracy permanent rather than towards furnishing the best available medical care to the most people.

Finally, he pointed out, no such system gives the worker anything beyond what he pays for himself since his contribution is deducted from his wages, his employer's contribution is added to the cost of the goods that the worker buys, and the government's contribution paid for through taxes on the worker. Thus, he concluded, the government does for him what he has been used to doing for himself but requires two additional employees for every doctor used in the service and gives him a lower quality of care.

President of M. H. A. Endorses Blue Shield

Dr. Charles F. Wilinsky, president of the Massachusetts Hospital Association, and chief medical officer for civilian defense, gave his full endorsement to the Blue Shield, the newly launched plan for prepaid budgeting of medical care established by the Massachusetts Medical Society.

Describing the plan as a great milestone in medical practice, Dr. Wilinsky said:

"The Blue Shield is what the public has been waiting for. Americans want to pay their own way and now, for the first time, the lower-income groups will be assured the best medical skill regardless of their financial circumstances."

The phenomenal increase in the number of Blue Cross hospital plan subscribers proves beyond a doubt, he said, that the citizens of Massachusetts want to protect themselves against the devastating cost of illness through a system of voluntary budgeting.

Speaking for the hospitals of the state, Dr. Wilinsky said that their directors and staffs would give full cooperation to the medical profession, the Blue Shield and the public in furthering the success of the project.

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Physician Participation

3,072 Massachusetts doctors had become participating physicians in the Massachusetts Medical Service prior to December 8. This impressive number is evidence of a professional unity which goes far toward assuring public acceptance of the Blue Shield.

The enthusiasm with which the public has welcomed the opportunity to protect itself through Blue Shield membership has lived up to all expectations. Many large companies have already indicated a desire to cooperate in the formation of employee groups. Steps are now being taken to enroll these groups.

Governor Praises Blue Shield

Governor Saltonstall, who has been a staunch supporter of the Blue Shield from its inception, issued a statement which appeared in newspapers throughout the state. A reprint from the *Springfield Union* follows.

Governor Urges All to Take Advantage of Benefits

Special to The Springfield Union

BOSTON, Nov. 22—Gov. Saltonstall today expressed gratification at the first week's applications for enrollment in the new Blue Shield plan for prepaid budgeting of medical care and urged all Massachusetts citizens to join, not only to their own benefit, but also as a health measure strengthening the wartime home front.

"Officers of the Blue Shield have informed me that the applications for enrollment during the first week which this service has been available to the public has even exceeded expectations," the Governor said. "This is good news and I trust is an indication of the greater numbers still to follow. I cannot too strongly urge all our citizens to take advantage of this program which was authorized by the Legislature with my hearty indorsement. It means less medical expense and better health for the average man, both of which factors are especially important in wartime when the strength of our home front is vital."

The Blue Shield Progresses

The rapidity with which doctors became participating physicians in the Blue Shield shows that the profession is well aware of current needs and dangers. Sir William Beveridge's plan containing social security provisions for virtually every person in Britain from the cradle to the grave, and calling for comprehensive medical care for all members of insured families, is a weathervane to future possibilities. This plan, coupled with Vice-President Wallace's assertion that "freedom from disease" must be added to the four freedoms, is promise enough that purely economic determinants can engulf and destroy our free American profession.

Whatever the outcome, it will be directly related to the profession's capacity as a socially-adjusted, self-disciplined group, to seek out and meet more effectively the need for a less costly distribution of proper medical care. Blue Shield represents the initial step in our first coordinated, officially sponsored effort to achieve this end.

The Blue Shield will continue to solicit physician participation without exerting pressure. To this end, the lay agents of the Blue Shield, through the channel of the Local Professional Service committees, will contact all physicians who intend to participate but who have forgotten to respond.

The Blue Shield corporation is functioning satisfactorily according to the pattern laid down by the committees and council of the Massachusetts Medical Society. The five physicians, who compose the Central Professional Service committee, and who, alone, are empowered in the by-laws to initiate all action on basic medical matters, have procured complete acceptance of the planned program by the Board of Directors. The President of the corporation reported the progress of the corporation to the Council in October. In the near future the Central Professional Service committee will meet with the Voting Members (the Executive Committee of the Medical Society).

Two weeks ago the Central Professional Service committee met and discussed many pertinent problems with the chairmen of the Local Professional Service committees from the Districts. The chairmen raised questions which have repeatedly confronted them. A few of these questions with brief answers are appended:

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*A New Type of Medication to Be Used in Bronchial Asthma and Other Allergic Conditions. *New England Journal of Medicine* 223:843-846, 1940.

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